

Fundamentals
INORGANIC
ORGANIC
& BIOLOGICAL
CHEMISTRY

By Joseph I. Routh, Ph.D.
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Second Edition, Illustrated

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PHILADELPHIA

To My Wife

THE NURSE WHOSE IDEAS AND
EXPERIENCE MADE THIS BOOK POSSIBLE



Preface to Second Edition

IN THE preparation of the second edition of this book the author has been guided by the suggestions and criticisms of other instructors who have used and evaluated the first edition.

The application of biochemistry to the practice of medicine and nursing has continued to increase in importance. For this reason and to present a more complete picture of biochemistry a new chapter on blood has been added to this section. The recent advances in the metabolism of fatty acids and acetone bodies have been incorporated in the chapter on the metabolism of the lipids. The material on the newer members of the vitamin B family has been revised to include recent knowledge. Folic acid has been added to this group of vitamins.

Revision of the inorganic and organic sections has not been as extensive although the material on atomic structure and isotopes has been altered. A discussion of radioactive isotopes, nuclear fission, and atomic energy has been included to provide a background for the understanding of the application of isotopes in the field of medicine. Several new illustrations have been added to these sections to serve as visual aids in the presentation of fundamental principles of chemistry.

In general, an attempt has been made to improve the discussion of several important topics in chemistry and to incorporate recent knowledge in these discussions.

The author is particularly pleased to acknowledge the valuable assistance gained from the suggestions and criticisms received from nursing instructors and administrators. Finally, he wishes to thank his publishers for their many suggestions and their welcomed assistance in the preparation of the manuscript.

JOSEPH I. ROUTH



Preface

THIS book is written expressly for students in an attempt to present the material that is most useful and interesting to them. Previous courses in chemistry are not necessary for the understanding of the material, although those students who have had high school chemistry will find that a review of the inorganic section will better enable them to master the organic and biochemistry sections that follow.

The author has felt that in the past there was an improper selection of material from inorganic, organic, and biochemistry in the majority of the textbooks of chemistry for nurses. The tendency has been to develop the inorganic chemistry to such an extent that organic and biochemistry are covered too briefly. The recent advances in biochemistry and their widespread application to the practice of medicine and nursing have considerably altered the situation. Not only is biochemistry more closely allied to the practical chemistry of medicine and nursing but it is also of more interest to the student. In the author's experience the response to biochemistry has always been more favorable than to the other sections. Within the brief period allotted to chemistry, therefore, the sections on inorganic, organic, and biochemistry should be so arranged that a good share of the time is spent in the study of biochemistry. This book presents mainly those fundamentals of inorganic and organic chemistry that are necessary for the understanding of the section on biochemistry.

An attempt has been made throughout the book to stress fundamental principles. Wordy definitions have been avoided to discourage memorization without understanding. Essential terms and principles have been set in *Italic type* to call attention to their importance.

The fundamental points suggested in the Curriculum Guide

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are included in the book, with some additions in the biochemistry section. The author feels that a study of urine, vitamins, nutrition, and hormones is so obviously a part of biochemistry that at least the fundamentals should be included in this course.

The book has been planned in such a way that it may be adapted to various courses in chemistry. The material suggested by the Curriculum Guide is covered in the first nineteen chapters and may be used in accelerated courses or where minimum time is allotted to chemistry. When the time allotted to the course is sixty to ninety hours the entire contents of the book may be used to advantage. While the book has been written especially to fit the needs of Schools of Nursing it could readily be applied in instances where students are required to take but one course in chemistry. The apathetic attitude of nonprofessional students toward a course in inorganic chemistry may well be overcome by the proper presentation of material selected from inorganic, organic and biochemistry.

The author takes special pleasure in acknowledging the valuable assistance in the preparation of the manuscript given by Mrs. J. Hummel, Mr. M. Heinrich, and Mr. J. Van Pilsum. He is indebted to Miss Lois Lindsey, Educational Director of the University of Iowa School of Nursing, and Sister M. Philomena, Superintendent of Nurses of Mercy Hospital School of Nursing, for their suggestions and encouragement to write the book. Thanks are due Mr. J. Hummel for the preparation of several illustrations and for his advice and criticism of the manuscript. Finally, the author wishes to express his appreciation to his publishers for their valuable suggestions and constant interest in the preparation of the manuscript for publication.

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CHAPTER I

Introduction

THE greatest advances in medical science are now chemical, whereas previously they were more biological in nature. The rapid development and widespread use of the sulfa drugs is but one of the many examples of the chemist's skill. At present the new product, penicillin, is proving more effective than the sulfa drugs in combating certain infections. Hundreds of chemists are studying the chemical nature and methods of preparation of this valuable therapeutic agent. The extensive use of vitamins and vitamin preparations has recently stimulated common interest in nutrition. This popular wholesale vitamin therapy has been made possible only by the ability of the chemist to manufacture pure vitamins in large quantities.

HISTORY OF CHEMISTRY

In an attempt to trace the origin of chemistry, we are carried back to the very beginning of civilization. It is said that chemistry originated in the Egyptian temples where priests experimented in the preparation of medicines.

From early records, it appears that alchemy, the attempts to transmute the base metals into silver and gold, had its origin in the Greek colony of Alexandria at the beginning of the Christian era. When the Arabians overran Egypt in the seventh century, they learned about chemistry from the Egyptians. Alchemy was carried into Spain by the Arabians, and by the fourteenth century its study extended throughout the civilized world. In a broad sense alchemy represents the chemistry of the Middle Ages.

In the sixteenth century, a new era of medical chemistry

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The development of both chemistry and medicine was given a healthy impetus by the doctrines of Paracelsus and the iatrochemists.

DIVISIONS OF CHEMISTRY

The two major divisions of chemistry are *inorganic* and *organic*. Inorganic chemistry is concerned with a study of lifeless material such as metals and minerals, and includes all elementary substances except carbon. Organic chemistry is a study of the matter which is closely associated with living things. Essentially, it is a study of compounds that contain carbon. Several important subdivisions of inorganic and organic chemistry have been developed, as analytical, physical, and biological chemistry.

IMPORTANCE OF CHEMISTRY

A reasonable knowledge of chemistry enables us to understand the millions of chemical changes that are constantly occurring. Our main interest is a consideration of the chemistry of the body in health and disease. The food we eat is an important weapon in the proper treatment of many abnormal conditions in the body. An acquaintance with the chemical nature of food and the chemical processes of digestion, absorption, and metabolism will increase your value as a nurse.

The majority of diseases are treated with chemicals called *drugs*, which change the chemical reactions in the body in an attempt to restore normal conditions. A better understanding of the effect of drugs may be gained through application of your knowledge of chemistry. It is a well-known fact that drugs are valuable agents in the treatment of disease, but they may be exceedingly harmful when administered promiscuously in the form of patent medicines. The American people find it difficult to resist the temptation of self-medication and pay millions of dollars each year for preparations whose continued use may produce harmful effects.

The present-day progress of medical science is very rapid, and a great share of this progress is due to the skill of the

began, marked by the advent of the iatrochemist, or physician chemist. This group of chemists believed that the prime purpose of chemistry was to prepare medicines and not to transmute base metals into gold. The most renowned of the medical chemists was Paracelsus, the son of a Swiss physician. He erroneously



Fig. 1. An ancient apothecary. (Courtesy of the Fisher Scientific Company, Pittsburgh.)

believed that man is made of sulfur, mercury, and salt, and the health of the body depended upon the correct proportion of these substances. A change in the proportion caused illness, which could be cured by the administration of chemical medicines. He was an advocate of careful observation in his practice

of medicine and discounted the earlier beliefs and superstitions of medical lore.

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research chemist. Hence, a basic knowledge of chemistry will enable you to keep abreast of recent medical discoveries made through chemistry.

The human body has often been referred to as a laboratory in which chemical changes are constantly occurring. To run the gamut from birth to death involves more reactions than are understood at the present time. Nevertheless, a knowledge of the fundamental principles of the chemical changes that occur in the body will enable you as a nurse to treat diseases of the body more intelligently.

SUGGESTED METHOD OF STUDY

Chemistry is a science and its study, like any other science, requires a different method of approach than the liberal arts courses with which we are familiar. Many of you are just beginning a study of chemistry while others may have had chemistry in high school and a few may have taken a course in college chemistry. Your attitude toward chemistry depends not only on your previous experience in the subject, but may be influenced to a large extent by the opinion of other students. The familiar hue and cry that chemistry is a "tough" course and should be avoided like the plague is heard on every campus. Many of you may feel rather apprehensive because you are required to take a course in chemistry. But it is a well-known fact that fear can be overcome by knowledge, and the study of chemistry is certainly no exception to this rule.

By far the most universally accepted method of study of students in grade school, high school, and college is memorization. Most of us are endowed with the mental ability to memorize facts, and details concerning the facts. In grade school, the facts were made interesting and repeated so often that they were relatively easy to memorize. In high school, a premium was placed on your ability to memorize, and your knowledge, when measured as grades, varied directly with your powers of memorization.

You are now faced with an entirely different task, that of learning a specific profession. Many of the courses which you

will take, as chemistry, physiology, bacteriology, pharmacology, and so on, are professions within themselves and require years of study for their mastery. Thus, you will soon find that it is impossible to memorize all the facts and details that are known about any one scientific subject. If you attempt to learn chemistry as you did History, Latin, or English in high school your mind will become confused with nonessential details.

How, then, should we approach the study of chemistry? It is realized that each individual has different methods of learning and that no single plan of study could be adopted by everyone. In chemistry, as in any other science, there are certain fundamental principles or concepts upon which large masses of detail are based. If we thoroughly understand the underlying principles, we can readily illustrate the principle with several individual chemical reactions. Even your instructors are unable to remember all the details of individual reactions.

Chemistry cannot be understood by merely reading an assigned section in a textbook. It requires a little more effort to recognize the fundamental principles upon which each section is based, but it results in an understanding that can never be achieved by memorization. A good study habit to develop early in your professional life is to prepare an outline of the most important points that are covered in your lecture and reading material. If you understand the subject, it will be easy to condense the principal thoughts into outline form. *Literally speaking, study with a pencil in your hand and use it constantly to practice formulas and equations that illustrate fundamental facts.* Another good study habit whose importance cannot be stressed too strongly is that of consistent application. Even though the temptation to let a course "slide" for a week or two is sometimes irresistible, it is a pernicious habit and should not be allowed to develop. You will find that the practice of studying for each session of a course as they occur throughout the week pays dividends in increased knowledge, self-confidence, and better grades. In any course, make an effort to recognize the important points that are stressed, without getting lost in a mass of details.

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CHAPTER II

Some Fundamental Concepts

CHEMISTRY is the science which deals with the composition of substances and with the changes which they may undergo. All substances are forms of matter, and *matter* is anything that possesses weight and occupies space. Matter exists in three states: solid, liquid, and gaseous, depending on the temperature and pressure. The relationship between matter and energy is very close. *Energy* is defined as the ability to do work. It exists in many different forms, each of which may be converted into any of the other forms. Heat, light, motion, sound, and electricity are all familiar forms of energy. *Chemical energy* is the energy that is stored up in chemical substances, and is released during chemical changes. Sometimes these energy changes become the most important part of a chemical reaction; for example the combustion of fuel in the furnace to produce heat or the "burning" of foods in the body to produce heat and energy. It should be kept in mind that every chemical change is accompanied by a change in energy.

PHYSICAL AND CHEMICAL PROPERTIES

We usually recognize substances by their appearance, taste, odor, feel, and other characteristics which serve to identify them. These characteristics are called the properties of the substance and are divided into two classes: physical and chemical. *Physical properties* are concerned with substances as they exist in nature; however the chemical properties of a substance are made manifest only when the substance undergoes a chemical change. Such characteristics as the physical state (solid, liquid or gaseous), crystalline form, odor, taste, color, luster, and

solubility are common physical properties. The *chemical properties* of a substance are characteristic of the manner in which they react with other substances, e.g., oxygen, water, acids, and bases.

Properties, then, are the signs by which we recognize substances. If we study the physical and chemical properties of two substances and find they are identical, then the substances must be the same, if the properties are different, we are concerned with two different substances.

CHEMICAL COMPOSITION

When we consider the composition of a substance, we are not concerned with its properties but with the simpler substances that have combined to make it. Water may be decomposed into constituents called hydrogen and oxygen; sugar into hydrogen, oxygen, and carbon; common salt into sodium and chlorine. The study of the simple substances that combine to form more complex ones, and the proportions in which they combine to form these substances, is an important part of elementary chemistry.

PHYSICAL AND CHEMICAL CHANGE

Substances are constantly undergoing physical and chemical changes. *Physical changes* are changes in the condition or state of a substance; they do not result in the formation of new substances nor involve a change in composition. An example of a physical change would be the breaking of a bottle. Although there has been a marked change, the substance is still glass. No new substance has resulted, nor have we produced a change in the composition of the glass. If we file a piece of iron into small pieces, we observe a definite change; yet the particles are readily identified as iron for they have the same properties as the original piece.

If we expose the iron filings to moisture, however, the iron will soon be changed into rust. A magnet will no longer attract the particles, the metallic luster is gone, the properties are different from those of the original substance; we therefore con-

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stances that are present. Most of our foods—meat, vegetables, and fruits—are mixtures, as are many medical preparations. Air is a very important mixture, consisting mainly of the gaseous elements oxygen and nitrogen.

THE METRIC SYSTEM

It is always rather confusing for those beginning the study of a scientific subject to be introduced to a system of measurement that differs from our ordinary system. The *metric system* is used by the scientist for weights and measures; the units of temperature are expressed as degrees centigrade. It is more convenient because it is a decimal system in which the divisions and multiples are in a ratio of tens. A great deal of confusion would be avoided if the metric system could be adopted by everyone.

The standard unit of length is called the *meter*, which was originally based on one ten-millionth of the distance from the equator to the north pole. The meter is equivalent to 39.37 inches. The *centimeter* is one-hundredth the length of a meter; the *millimeter* is one-thousandth of a meter or one-tenth of a centimeter. There are approximately 30 centimeters in a foot or about 2.5 centimeters in an inch.

These units of length are abbreviated: m. (meter), cm. (centimeter), and mm. (millimeter), and their relation to each other can be stated simply as follows: $1 \text{ m.} = 100 \text{ cm.} = 1000 \text{ mm}$

The standard unit of weight is the *kilogram*, which is the weight of a block of platinum-iridium kept by the International Bureau of Weights and Measures. A kilogram weighs approximately 2.2 pounds. The *gram* is one-thousandth the weight of a kilogram and the milligram is one-thousandth the weight of a gram. These units are abbreviated as follows: kg. (kilogram), gm. (gram), and mg. (milligram). In modern vitamin therapy, quantities are often expressed in micrograms. A microgram is one-thousandth of a milligram and is abbreviated $\mu\text{g.}$, often called a gamma. We may represent these relationships as follows: $1 \text{ kg.} = 1000 \text{ gm.}; 1 \text{ gm.} = 1000 \text{ mg.}; 1 \text{ mg.} = 1000 \mu\text{g.}$

The *liter* is the unit of volume; it is the volume occupied by

clude that a new substance has been formed. When we heat a piece of wood in a test tube, we observe that dense fumes are formed and a black charred mass remains behind. The rusting of iron and the destruction of wood by heat are examples of chemical changes. We might then define *chemical changes* as those that result in the formation of new substances and involve changes in the composition of the substance.

ELEMENTS, COMPOUNDS, AND MIXTURES

All of the chemical substances we know may be divided into three classes: elements, compounds, and mixtures. *Elements* are certain substances so elementary that they cannot be made simpler by ordinary chemical methods. There are 96 of these elements, and they are considered the basic forms of all matter. Iron, oxygen, gold, neon, copper, and nitrogen are examples of elements.

By proper combination of these basic substances, we may prepare thousands of more complex substances. These substances are called *compounds* and are composed of two or more elements combined chemically and in definite proportions. If a compound is decomposed or broken down into its constituent elements, we can determine its composition. Water may be decomposed into its constituents, the elements hydrogen and oxygen, by passing an electric current through it. Iron rust, which is iron oxide, may be broken down into its constituent elements, iron and oxygen, by a suitable chemical procedure. It will be shown later that every chemical compound contains its constituent elements in definite proportions by weight. A given amount of water always contains a definite amount of hydrogen combined with a definite amount of oxygen. In this way, we can readily recognize any chemical compound if we know its composition.

The remaining class of substances is called *mixtures*. A mixture is made up of two or more substances that are not combined chemically and may be present in any proportion. The ingredients in a mixture can usually be separated by physical methods without changing the chemical identities of the individual sub-

We are accustomed to expressing temperature measurements on the common Fahrenheit scale. On this scale, the temperature at which water freezes is 32 degrees (32°), while water boils at 212° F. In scientific work, this system has been replaced by the simpler centigrade scale, which is based on the freezing and boiling points of water. The freezing point was taken as 0° C. and the boiling point as 100° C.

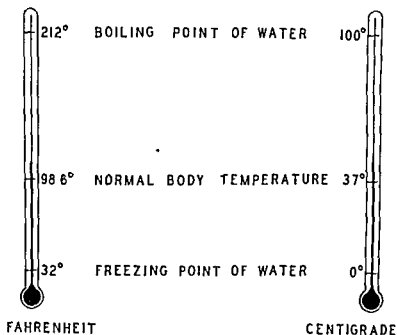


Fig. 2. A comparison of the Fahrenheit and centigrade thermometers.

A temperature on one scale may readily be converted to the corresponding temperature on the other scale. To convert degrees Fahrenheit to degrees centigrade: add 40, multiply by $\frac{5}{9}$, and subtract 40 from the result. As an example, let us convert 32° F. to degrees centigrade:

$$\begin{array}{rcl} 32^{\circ} \text{ F.} & + 40 & = 72 \\ 72 & \times \frac{5}{9} & = \frac{360}{9} = 40 \\ 40 & - 40 & = 0^{\circ} \text{ C.} \end{array}$$

To convert degrees centigrade to degrees Fahrenheit: add 40, multiply by $\frac{9}{5}$, and subtract 40 from the result. For example, let us convert 100° C. to degrees Fahrenheit:

a kilogram of pure water at 4° centigrade (the temperature at which a volume of water weighs the most). A liter is slightly more than a quart. A milliliter is one-thousandth of a liter and is approximately the same as a *cubic centimeter*. Ordinarily we say that a liter is equal to 1000 cubic centimeters. A fluid ounce is approximately 30 cubic centimeters; a teaspoon holds about 4 cubic centimeters. The units of volume are abbreviated as follows: l. (liter), ml. (milliliter), and cc. (cubic centimeter).

The units of the metric system may be represented in tabular form as follows:

UNITS OF LENGTH

Millimeter	=	0.001 meter
Centimeter	=	0.01 meter
Decimeter	=	0.1 meter
Meter	=	1.0 meter
Dekameter	=	10 meters
Hectometer	=	100 meters
Kilometer	=	1000 meters

UNITS OF WEIGHT

Microgram	=	0.001 milligram
Milligram	=	0.001 gram
Gram	=	1.0 gram
Kilogram	=	1000 grams

UNITS OF VOLUME

Milliliter	=	0.001 liter
Liter	=	1.0 liter

SOME APPROXIMATE EQUIVALENTS

1 inch	=	2.5 centimeters
1 foot	=	30 centimeters
1.1 yard	=	1 meter
15 grains	=	1 gram
1 avoird. ounce	=	30 grams
1 pound	=	450 grams
2.2 pounds	=	1 kilogram
1 fluidounce	=	30 cubic centimeters
1 quart	=	950 cubic centimeters
1 teaspoon	=	4 cubic centimeters
1 tablespoon	=	15 cb. = $\frac{1}{2}$ fluidounce

CHAPTER III

Atoms and Molecules

As we have already seen, the vast number of compounds known to the chemist are built from the basic substances, elements. Experiments have shown repeatedly that when elements combine to form compounds, a definite weight of each element always unites with a definite weight of the other elements.

ATOMIC THEORY

The early Greek philosophers reasoned that repeated division of matter would ultimately end in chemically indivisible particles, to which they gave the name "atoms." These speculations and observations were known to the English scientist, John Dalton, who in 1804 proposed a theory to explain them. His ideas were generally accepted and are known as the *atomic theory*. He began by assuming that all elements are composed of minute invisible particles called *atoms*. The atom may then be considered the smallest unit of an element, and since there are 96 different elements, it is reasonable to assume that there can be only 96 different atoms. Dalton stated further that all atoms of the same element had the same properties and the same weight, but that they differed from the atoms of all the other elements in these respects. In chemical changes, the atoms could combine to form small particles of compounds, or they could separate or change places in these compounds. When the atoms enter into chemical combination, the weight of the individual atoms does not change.

We may, therefore, regard an atom as the smallest particle of an element that can take part in a chemical change.

$$100^{\circ} \text{C.} + 40 = 140$$

$$140 \times \frac{5}{9} = 122\frac{2}{3} = 252$$

$$252 - 40 = 212^{\circ} \text{F.}$$

Other methods of conversion from one temperature scale to another may be used, although the one explained seems easier to remember. In both conversions, you add 40 to the original temperature, multiply by either $\frac{5}{9}$ or $\frac{9}{5}$ and subtract 40 from the result. If you choose a common point like the boiling point of water, 212°F. and 100°C. , it can be seen that the Fahrenheit value is higher than the centigrade; therefore, you would have to use the largest factor $\frac{9}{5}$ to convert centigrade to Fahrenheit. Conversely, since the centigrade value is lower than the Fahrenheit, you would use the factor $\frac{5}{9}$ to convert Fahrenheit to centigrade.

REVIEW QUESTIONS

1. Name several instances in which electrical energy is converted into other forms of energy for use in the hospital.
2. List several of the physical properties that would be helpful in the identification of the following substances: iron, copper, ether, lead, charcoal, gasoline, and silver.
3. How do you distinguish between a physical and a chemical change?
4. Which of the following are physical changes and which are chemical changes?

Lighting a match	Chopping wood
Boiling water	Souring of milk
Making a cake	Frying of meat
Ripening of fruit	Breaking a plate
5. Give three examples of the use of uncombined elements in medicine.
6. Differentiate between compounds and mixtures.
7. A 3-inch bandage is equivalent in width to how many millimeters?
8. What is the weight in kilograms of a 10-pound plaster cast?
9. What is the volume of an 8-ounce glass, expressed in cubic centimeters?
10. Room temperature is usually about $75^{\circ} \text{Fahrenheit}$. What would be the reading on the centigrade scale?
11. Dry ice has a temperature of $-80^{\circ} \text{centigrade}$. This is equivalent to what temperature on the Fahrenheit thermometer?

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We may, therefore, regard an atom as the smallest particle of an element that can take part in a chemical change.

ATOMIC WEIGHT

A single atom is so small that it would be impossible to weigh it accurately. It has been possible, however, to weigh large groups of atoms that contain equal numbers of any one atom and in this manner the relative weights of atoms of different elements have been determined. The 96 different atoms could then be arranged in order of their relative weights. Such a series would be useful if the *atomic weight* of each atom could be expressed as a numerical value. Oxygen was used as a standard reference element because it is the most abundant, and is one with which almost all the other elements will combine. An atom of oxygen was found to be approximately 16 times as heavy as the lightest atom, hydrogen, so its atomic weight was set at 16. The atomic weight of hydrogen then became 1.008. It was determined that an atom of nitrogen weighed $\frac{14}{16}$ as much as an atom of oxygen, giving it an atomic weight of 14. The sulfur atom was twice as heavy as the oxygen atom, therefore sulfur has an atomic weight of 32. A complete table of atomic weights will be found in the Appendix.

MOLECULES

The atomic theory states that in chemical changes the atoms can combine to form small particles of compounds. Each small particle of a compound contains a definite number of

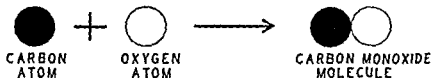


Fig. 3. The union of an atom of carbon with an atom of oxygen to form a molecule of carbon monoxide.

atoms. This means that each unit particle of a compound must have the same number and kinds of atoms as all the other unit particles. These small unit particles of which every compound is composed are called *molecules*. The molecule can be considered the indivisible unit for compounds, much as the atom is the unit particle for elements.

The simplest compound would be one whose molecule contains one atom of each of the two elements that unite to form the compound. An example of such a simple compound is carbon monoxide (Fig. 3), whose molecule is composed of 1 atom of carbon and 1 atom of oxygen. Every molecule of water contains 2 atoms of hydrogen and 1 atom of oxygen.

The majority of molecules are composed of two or more different atoms; however, some atoms of the same element are capable of uniting with each other to form a molecule of that element. This is particularly true of elements that are gases at room temperature (oxygen, hydrogen, nitrogen, and chlorine). Such gases always exist in molecular form when in the free state, each molecule containing 2 atoms of the element. For example a molecule of oxygen may be represented as in Figure 4.

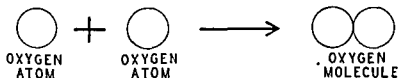


Fig. 4. The union of two oxygen atoms to form a molecule of oxygen. Like most gases, oxygen is found in nature in this molecular form.

This combination of atoms to make molecules of gas is very important in chemical reactions in which a gas such as oxygen or hydrogen is formed.

MOLECULAR WEIGHT

The *molecular weight* of a compound is the sum of the atomic weights of all the atoms present in one molecule of the compound. A molecule of carbon dioxide contains 1 atom of carbon and 2 atoms of oxygen. Since the atomic weight of carbon is 12 and the atomic weight of oxygen is 16, the molecular weight may be calculated as follows.

ELEMENT	ATOMIC WEIGHT
Carbon	12
Oxygen ..	16
Oxygen. ..	16
Carbon dioxide.....	44 = Molecular weight

ATOMIC WEIGHT

A single atom is so small that it would be impossible to weigh it accurately. It has been possible, however, to weigh large groups of atoms that contain equal numbers of any one atom and in this manner the relative weights of atoms of different elements have been determined. The 96 different atoms could then be arranged in order of their relative weights. Such a series would be useful if the *atomic weight* of each atom could be expressed as a numerical value. Oxygen was used as a standard reference element because it is the most abundant, and is one with which almost all the other elements will combine. An atom of oxygen was found to be approximately 16 times as heavy as the lightest atom, hydrogen, so its atomic weight was set at 16. The atomic weight of hydrogen then became 1.008. It was determined that an atom of nitrogen weighed $\frac{1}{14}$ as much as an atom of oxygen, giving it an atomic weight of 14. The sulfur atom was twice as heavy as the oxygen atom, therefore sulfur has an atomic weight of 32. A complete table of atomic weights will be found in the Appendix.

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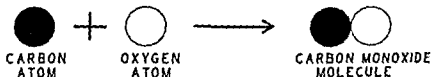


Fig. 3. The union of an atom of carbon with an atom of oxygen to form a molecule of carbon monoxide.

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44 gm. of carbon dioxide contains the same number of molecules as 62 gm. of carbonic acid or 18 gm. of water. This law has a practical application in expressing the concentration of solutions.

THE STRUCTURE OF THE ATOM

Atoms are made up of positive electrical units called *protons*, and negative electrical units called *electrons*. Any one atom contains the same number of electrons as it does protons. A third type of particle called the *neutron* is also present in the atom. Each neutron consists of one proton and one electron, and is therefore electrically neutral.

Every atom consists of a *nucleus* surrounded by electrons which revolve about it at relatively great distances, much as the planets revolve about the sun. The nucleus is a small, compact mass made up of protons and neutrons. It is positively charged because it contains a number of free protons in excess of those combined with electrons in neutrons. Since atoms contain an equal number of electrons and protons, the number of electrons revolving around the nucleus must be exactly equal to the excess protons in the nucleus. The nitrogen atom, for example, has 7 electrons revolving around its nucleus; therefore, it must have 7 uncombined protons (positive charges) in the nucleus.

The number of revolving or "*planetary*" *electrons* in an atom is equal to the *atomic number* of the atom. The excess positive charges (protons) in the nucleus are also equal to the atomic number. If we are told that the atomic number of oxygen is 8, we can conclude that the oxygen atom has 8 planetary electrons and 8 uncombined protons in the nucleus.

The mass of an atom consists almost entirely of the heavy protons and neutrons in the nucleus. Electrons possess a negligible mass, $\frac{1}{1836}$ that of a proton, and may be disregarded in a consideration of the weight of an atom. Each proton or neutron contributes one unit to the weight of the atom. The *atomic weight* of an atom is thus equal to the total number of protons and neutrons in the nucleus.

A molecule of carbonic acid contains 2 atoms of hydrogen, 1 atom of carbon, and 3 atoms of oxygen. The atomic weight of hydrogen is ordinarily taken as 1 in chemical calculations. The molecular weight of carbonic acid is 62 as shown by the calculation:

ELEMENT	ATOMIC WEIGHT
Hydrogen	1
Hydrogen	1
Carbon.	12
Oxygen.	16
Oxygen.	16
Oxygen	16
Carbonic acid.	62 = Molecular weight

Each atom of hydrogen, carbon, or oxygen in these compounds has a weight of its own and must be used in a calculation of the molecular weight each time it occurs in the compound.

If the molecular weight of a compound can be represented as the sum of the atomic weights of all the atoms in the molecule, then every compound must have a constant composition. A compound is always made up of definite proportions by weight of its constituent elements; this is known as the *law of definite proportions*. For example, specimens of water collected from any source always contain 2 parts by weight of hydrogen to 16 parts by weight of oxygen. If water is formed from a mixture of hydrogen and oxygen gas, the compound formed will always contain 2 parts of hydrogen to 16 parts of oxygen by weight, and any excess of hydrogen or oxygen gas will remain uncombined.

The atomic weight of an element or the molecular weight of a compound may be expressed in any units. If they are expressed in grams, we have the *gram atomic weight* of the element and the *gram molecular weight* of the compound. Therefore, the gram molecular weight is the sum of the gram atomic weights of the atoms in the molecules. Thus, carbon dioxide has a gram molecular weight of 44; carbonic acid, 62; and water, 18. Avogadro, an Italian physicist, stated that a gram molecular weight of any compound contains the same number of molecules as a gram molecular weight of any other compound. This means that

is 23. Atoms of elements with higher atomic weights can be illustrated in a similar fashion, but become more and more diffi-

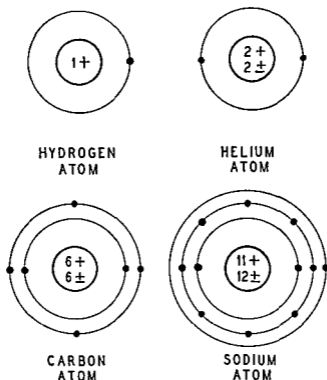


Fig. 5. The structure of the atoms of a few common elements.

cult to represent as they approach curium, which has an atomic weight of 242 and an atomic number of 96.

ISOTOPES

From inspection of the table of atomic weights in the Appendix, we can see that few elements have atomic weights that can be expressed in whole numbers. It is known that atoms of the same element show slight variations in their mass, because they have different numbers of neutrons in their nucleus. These atoms of different weights are called *isotopes*. The actual atomic weight of an element represents the average weight of its atoms. For example, there are two forms of hydrogen atoms, one heavier than the other but occurring less often than the ordinary hydro-

The planetary electrons revolve in concentric rings or shells about the nucleus in a fashion similar to that in which planets revolve in definite orbits around the sun. Only 2 electrons can occupy the shell or orbit closest to the nucleus. The next nearest shell can hold up to 8 electrons. As many as 18 electrons can occupy the third orbit.

The lightest atom, the hydrogen atom, has a nucleus of 1 proton with 1 planetary electron rotating about it in the first orbit. In the following figure, the nucleus is represented as a small circle, containing protons (+) and neutrons (=). The (+) represents the positively charged protons, while the (=) represents the union of a proton and an electron within the nucleus. Planetary electrons are shown as shaded circles and the orbit or shell in which they revolve as a large circle. The atomic number and atomic weight of hydrogen may readily be determined from the diagram. Since there is 1 planetary electron rotating about the nucleus, the atomic number is 1; the atomic weight is also 1 because there is 1 proton in the nucleus.

Helium, the second lightest element, has 2 protons and 2 neutrons in its nucleus, with 2 planetary electrons revolving in the first orbit. These two electrons complete this shell. By inspection of Fig. 5, we can see that helium has an atomic number of 2 and an atomic weight of 4 (2 protons + 2 neutrons).

Carbon is an example of an element whose planetary electrons rotate in the first and second orbits. Its nucleus contains 6 protons. Six planetary electrons rotate around the nucleus. Since the first orbit can hold only 2 electrons, the other 4 must revolve in a new orbit at a greater distance from the nucleus. A glance at the diagram reveals an atomic number of 6 and an atomic weight of 12 for carbon.

A more complicated atom such as sodium is also represented in Fig. 5. The nucleus consists of 11 protons and 12 neutrons with 11 planetary electrons rotating about it. As the first two shells are completely filled by 10 electrons, the remaining electron occupies the third orbit, which is still farther from the nucleus. The atomic number of sodium is 11, the atomic weight

is 23. Atoms of elements with higher atomic weights can be illustrated in a similar fashion, but become more and more diffi-

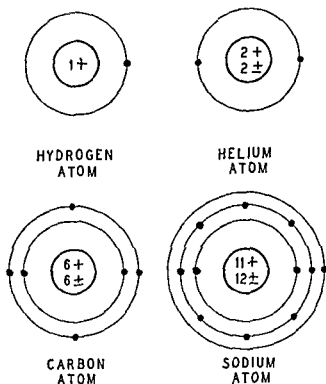


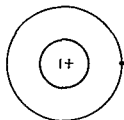
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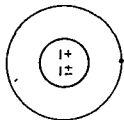
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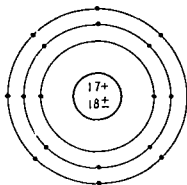
gen atom. An ordinary hydrogen atom has 1 proton, a heavy hydrogen atom has 1 proton and 1 neutron (Fig. 6). The mixture in naturally occurring hydrogen has an atomic weight of 1.008 compared to 1.0078 for the lighter form and 2.0143 for the heavier. This difference in weight is used as a basis for separation of isotopes from ordinary atoms. The heavy hydrogen atom is called



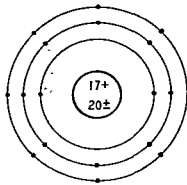
ORDINARY
HYDROGEN



HEAVY
HYDROGEN



ORDINARY
CHLORINE



HEAVY
CHLORINE

Fig. 6. A comparison of the structure of ordinary atoms and heavy atoms or isotopes.

deuterium, and water made of heavy hydrogen and oxygen is called "*heavy water*." All samples of water contain a small amount of heavy water.

Another example is heavy chlorine, which has 2 extra neutrons in its nucleus (Fig. 6). The chlorine gas that is used in water purification or in the laboratory is a mixture of ordinary

chlorine atoms and heavy chlorine atoms and has an atomic weight of 35.46. It should be stressed that *isotopes* are atoms that have different numbers of neutrons in their nuclei, therefore they have different weights than ordinary atoms. However, these isotopes have the same number of protons and electrons and behave alike chemically. All of the 96 elements have two or more isotopes, and about 300 stable isotopes have been found occurring in natural mixtures similar to hydrogen and chlorine.

RADIOACTIVE ELEMENTS

Since all of the elements are made of similar units, it is reasonable to assume that an attempt would be made to convert one element into another, to fulfill the dream of the alchemists. This has been accomplished with certain elements by bombarding the atoms with swiftly moving subatomic particles. Certain ores in nature contain elements that have the property of decomposing spontaneously into elements of smaller weight. Three of these elements, radium, thorium, and uranium, are known to disintegrate slowly into elements of lower atomic weights. In the process they emit positively charged *alpha particles*, which are identical with the nucleus of the helium atom; *beta particles*, which are rapidly moving electrons; and *gamma rays*, which are similar to x-rays, although they are more penetrating. These elements are said to be *radioactive*. In 1898, Madame Curie, in collaboration with her husband Pierre, discovered the element radium.

Radium is used in medicine to treat cancer because the rays it gives off seem to destroy cancerous tissue more rapidly than normal tissue. Thick lead containers are used to handle radioactive substances because they stop all the particles and rays that are emitted from it.

Artificial radioactive elements can be prepared by bombarding stable elements with rapidly moving subatomic particles. Elaborate electromagnetic generators have been built to accelerate the movement of alpha particles, beta particles, protons, and deuterons (the nucleus of deuterium atoms). The *cyclotron* developed at the University of California is probably the most

common particle accelerator, and consists of a huge electromagnet whose poles inclose a hollow, flat disk in which positively charged protons or deuterons are accelerated until they reach a speed of thousands of miles a second. These particles are directed



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Fig. 7. Marie Skłodowska was born in Poland in 1867. Her father, a professor of physics and mathematics in Warsaw, greatly influenced her early education. On moving to Paris she met and married Pierre Curie, then a graduate student at the University. Together they isolated polonium and later radium from pitchblende. For their work on radioactivity and their discovery of radium they shared in the 1903 Nobel Prize in Physics. After the death of her husband, in 1906, Mme. Curie succeeded him as professor of physics at the University of Paris.

at a target containing stable atoms whose nuclei are changed by the bombardment to produce *radioactive isotopes*. These isotopes are called unstable, or radioactive, because their nuclei are undergoing continuous disintegration with the release of energy and subatomic particles.

NUCLEAR FISSION

Large quantities of radioactive isotopes are also produced by the process of *nuclear fission*. In 1939, it was shown that when uranium was bombarded by neutrons, several other elements were formed and considerable energy was liberated. It was soon discovered that only one of the isotopes of uranium, U235 (uranium with an atomic weight of 235) was capable of being split into radioactive fragments with a release of energy. As the fission of U235 proceeded, several new neutrons were produced; and if these were passed through graphite, they were capable of splitting more U235 and a chain reaction was set up. If the chain

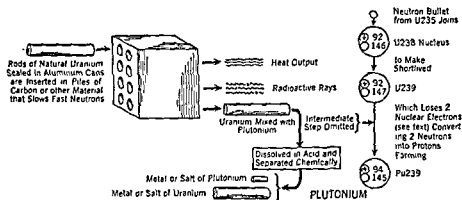


Fig. 8. A Schematic representation of an atomic pile. (From Chemistry for Our Times, by Weaver and Foster. 1947, McGraw-Hill Book Co., Inc.)

reaction was not controlled, the fission proceeded with such speed that a violent explosion occurred. For example, one pound of U235 could produce destruction equivalent to over 100 tons of TNT if only 5 per cent of the isotope was decomposed. The nuclear fission of U235 occurring in a chain reaction was the basis of the first atomic bomb.

Several attempts to produce a controlled chain reaction resulted in the construction of the *uranium pile* or reactor (Fig. 8). Graphite blocks and uranium metal were piled alternately in a cubical structure that contained several tons of these materials. Control rods of cadmium, a neutron-absorbing material, were

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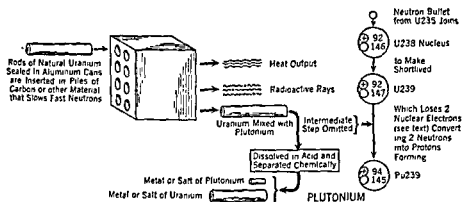


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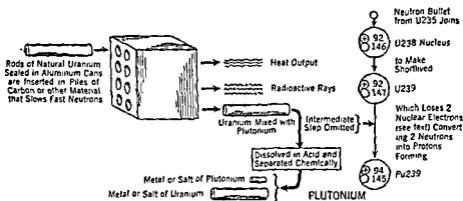


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inserted at intervals in the pile to keep the reaction at a reasonable rate. An extensive cooling system of circulating water was necessary to remove the heat produced by the chain reaction.

After the first pile was placed in operation, several interesting reactions and products were discovered. Two new elements, *neptunium*, atomic number 93, and *plutonium*, atomic number 94, were produced from the natural form of uranium U238. Later plutonium and uranium U238 were bombarded by alpha particles in a cyclotron to produce two more new elements, *americium*, atomic number 95, and *curium*, atomic number 96.

When it was discovered that plutonium as well as U235 would undergo nuclear fission and set up a chain reaction to produce enormous amounts of energy, large piles were constructed to manufacture stores of this element. The second atomic bomb used in Japan was a plutonium bomb.

Extensive programs are under way to study the possible use of atomic energy for power and heat and industrial purposes as well as the very important application of radioactivity in medical research.

Many biochemists and physiologists are studying reactions in the body with the help of radioactive isotopes. It is difficult to follow the course of any important compound throughout the various tissues in the body; however, if the compound contains a radioactive element, its pathway can readily be traced. Radioactive carbon, nitrogen, phosphorus, and sulfur have been incorporated in compounds and used as tracer elements to discover new facts about metabolism, and reactions in the tissues of the body. In medical research, radioactive iodine is being used in the treatment and study of disorders of the thyroid gland while radioactive strontium is used in a study of the healing of bone fractures. Several isotopes are being employed in a search for the proper treatment of cancer with encouraging results.

REVIEW QUESTIONS

1. State the main assumptions of the atomic theory.
2. Why was it necessary to obtain relative weights of atoms of different elements when atomic weights were first determined?

3. What element is used as a standard reference element in calculating atomic weights? Why?
4. How would you explain the difference between an atom and a molecule?
5. A molecule of carbon monoxide consists of 1 atom of carbon and 1 atom of oxygen. What is the molecular weight of carbon monoxide?
6. Name three elements that exist as gases at room temperature
7. Why can we speak of either an atom or a molecule of hydrogen, but only of an atom of carbon?
8. Sulfuric acid molecules are made up of 2 hydrogen atoms, 1 sulfur atom, and 4 oxygen atoms. Calculate the molecular weight of sulfuric acid.
9. Define electron, proton, and neutron
10. How could you determine the atomic number and the atomic weight of an atom from a diagram of its atomic structure?
11. The nucleus of the sulfur atom contains 16 protons and 16 neutrons. How many planetary electrons revolve about the nucleus? What would be the atomic number of sulfur? The atomic weight?
12. Nitrogen has an atomic number of 7 and an atomic weight of 14. Draw a diagram of the nitrogen atom.
13. What is the essential difference between an isotope and an ordinary atom?
14. What radioactive element has been used in medicine for several years? What conditions are treated with this element and why is it effective?
15. What are radioactive isotopes? Can they be made artificially? Explain
16. Name the four new elements that resulted from recent research in nuclear fission.

inserted at intervals in the pile to keep the reaction at a reasonable rate. An extensive cooling system of circulating water was necessary to remove the heat produced by the chain reaction.

After the first pile was placed in operation, several interesting reactions and products were discovered. Two new elements, *neptunium*, atomic number 93, and *plutonium*, atomic number 94, were produced from the natural form of uranium U238. Later plutonium and uranium U238 were bombarded by alpha particles in a cyclotron to produce two more new elements, *americium*, atomic number 95, and *curium*, atomic number 96.

When it was discovered that plutonium as well as U235 would undergo nuclear fission and set up a chain reaction to produce enormous amounts of energy, large piles were constructed to manufacture stores of this element. The second atomic bomb used in Japan was a plutonium bomb.

Extensive programs are under way to study the possible use of atomic energy for power and heat and industrial purposes as well as the very important application of radioactivity in medical research.

Many biochemists and physiologists are studying reactions in the body with the help of radioactive isotopes. It is difficult to follow the course of any important compound throughout the various tissues in the body; however, if the compound contains a radioactive element, its pathway can readily be traced. Radioactive carbon, nitrogen, phosphorus, and sulfur have been incorporated in compounds and used as tracer elements to discover new facts about metabolism, and reactions in the tissues of the body. In medical research, radioactive iodine is being used in the treatment and study of disorders of the thyroid gland while radioactive strontium is used in a study of the healing of bone fractures. Several isotopes are being employed in a search for the proper treatment of cancer with encouraging results.

REVIEW QUESTIONS

1. State the main assumptions of the atomic theory.
2. Why was it necessary to obtain relative weights of atoms of different elements when atomic weights were first determined?

ELEMENT	SYMBOL	ELEMENT	SYMBOL
Oxygen	O	Silver (argentum)	Ag
Phosphorus . .	P	Sodium (natrium)	Na
Platinum . . .	Pt	Sulfur	S
Potassium (kalium). . .	K	Zinc	Zn

For our purposes, it is not necessary to study each of the 96 elements, since many of them are quite uncommon. The common elements, with many of their chemical and physiological properties, are listed in two tables in the Appendix.

These symbols or abbreviations for the elements are more accurately called *atomic symbols* in that they stand for one atom of an element. In chemical reactions, they are often used to designate an atomic weight of an element. When expressed in grams, the symbol O, for example, means a gram atomic weight of oxygen, or 16 gm. In this way, N stands for 1 atom of nitrogen, 1 atomic weight, or 14 gm. of nitrogen. To indicate more than one atom the proper numeral is placed before the symbol, thus 5N represents 5 atoms of nitrogen, 5 gram atomic weights, or $5 \times 14 = 70$ gm. of nitrogen.

FORMULAS

A *formula* expresses in symbols the composition of a molecule of a substance. Since molecules are composed of atoms combined in definite proportions, we can represent a molecule by a combination of the symbols of the atoms. A molecule of common salt is composed of 1 atom of sodium and 1 atom of chlorine, and can be represented by combining the symbols for these elements into the formula NaCl. Where there is more than one atom of the same kind in the molecule, we do not repeat the symbol but indicate the number as a *subscript to the symbol* for the element. For example, the formula for water is written H₂O, meaning that 1 molecule of water contains 2 atoms of hydrogen and 1 atom of oxygen. The small subscript 2 which follows the H indicates that 2 atoms are present in the molecule. A molecule of sulfuric acid consists of 2 atoms of hydrogen, 1 atom of sulfur and 4 atoms of oxygen. Its formula may be written as follows:

CHAPTER IV

Valence and Chemical Equations

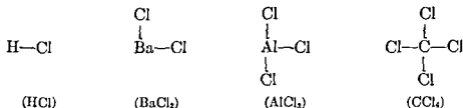
SYMBOLS

IN THE writing of chemical reactions, it is not convenient to write out the names of the elements. For this reason chemists use *symbols* to represent the elements. Some elements are represented by the first letter of the name; thus C stands for carbon, O for oxygen, N for nitrogen, and H for hydrogen. Since the names of several elements have the same first letter we sometimes add another prominent letter in the name to distinguish them, as Ba for barium, Ca for calcium, Br for bromine, and Cl for chlorine. Some elements were known in ancient times and had Latin names given to them. The symbols for these elements are taken from the Latin instead of the English name. Ferrum is the Latin name for iron, and the symbol is Fe; mercury is represented by the symbol Hg from the Latin name, hydrargyrum.

The symbols for some of the important elements are given in the following table. When the symbol is derived from the Latin name of the element, the Latin name is given in parentheses:

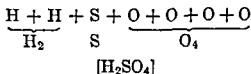
ELEMENT	SYMBOL	ELEMENT	SYMBOL
Aluminum	Al	Hydrogen	H
Barium	Ba	Iodine	I
Bromine	Br	Iron (ferrum)	Fe
Calcium	Ca	Lead (plumbum)	Pb
Carbon	C	Magnesium	Mg
Chlorine	Cl	Mercury (hydrargyrum)	Hg
Copper (cuprum)	Cu	Nitrogen	N

the other elements with it. We start by stating that the holding power of hydrogen for other atoms is 1. Or more simply stated, the valence of hydrogen is 1. One atom of hydrogen combines with 1 atom of chlorine. The chlorine atom and any other atom that unites with a hydrogen atom in a 1:1 ratio, also has a valence of 1. The barium atom is able to hold 2 chlorine atoms in combination, thus has a valence of 2. Aluminum unites with 3 chlorine atoms, giving it a holding power three times that of hydrogen, therefore its valence is 3. Carbon tetrachloride is a compound in which 4 chlorine atoms are held in combination with 1 carbon atom, hence the valence of carbon is 4. The formulas of these compounds may be used to illustrate valence as follows:

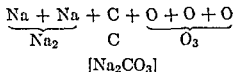


Each bond represents a holding power or valence of 1. In the ordinary empirical formulas given in parentheses, the number of chlorine atoms that combine with H, Ba, Al and C is given by the subscript following the Cl.

The elements are usually divided into two groups according to their valence. Any element that will combine with hydrogen, as chlorine, oxygen, etc., is said to have *negative valence*; hydrogen and elements that do not combine with hydrogen, as barium, aluminum, etc., are said to have *positive valence*. In general, all metals and hydrogen have a positive valence. The other elements or nonmetals usually have a negative valence. Each element with a positive valence is often labelled with a + over it for each positive valence or holding bond, as Na^+ , Ba^{++} , and Al^{+++} . The negative elements are likewise marked with a - sign for valences, as Cl^- , O^{--} , and S^{--} . A knowledge of the valence of elements is essential in writing the formula of a compound.



The formula H_2SO_4 represents 1 molecule, 1 molecular weight, or 1 gram molecular weight of sulfuric acid. The latter value equals the sum of the gram atomic weights of the atoms in the molecule, or 2 gram atomic weights of hydrogen plus 1 gram atomic weight of sulfur plus 4 gram atomic weights of oxygen. Sodium carbonate is composed of 2 atoms of sodium, 1 atom of carbon, and 3 atoms of oxygen; the formula may be illustrated as shown:



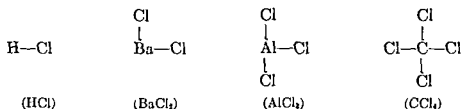
Again observe that the subscript numbers are written after the atomic symbols to which they belong. As we have already seen, the atoms of most gases do not exist by themselves but unite to form a molecule of the gas. The molecule of hydrogen is written H_2 , of nitrogen N_2 , and of oxygen O_2 .

To designate more than one molecule of a substance, we place the appropriate number in front of the formula. The term 3 NaCl represents 3 molecules of sodium chloride, 2 O_2 represents 2 molecules of oxygen gas, and 4 Na_2CO_3 represents 4 molecules of sodium carbonate. To avoid confusion of the subscript numbers and the numbers written in front of the formulas, it would be wise, at first, to write the full meaning of the different terms. For example, 3 H_2SO_4 , would read 3 molecules of sulfuric acid, each molecule consisting of 2 atoms of hydrogen, 1 atom of sulfur and 4 atoms of oxygen.

VALENCE

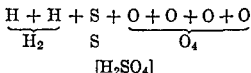
When atoms combine to form molecules, they unite in different proportions in different compounds. The property which an atom has of combining with other atoms is called its *valence*. Since hydrogen is the lightest element known, we often compare

the other elements with it. We start by stating that the holding power of hydrogen for other atoms is 1. Or more simply stated, the valence of hydrogen is 1. One atom of hydrogen combines with 1 atom of chlorine. The chlorine atom and any other atom that unites with a hydrogen atom in a 1:1 ratio, also has a valence of 1. The barium atom is able to hold 2 chlorine atoms in combination, thus has a valence of 2. Aluminum unites with 3 chlorine atoms, giving it a holding power three times that of hydrogen, therefore its valence is 3. Carbon tetrachloride is a compound in which 4 chlorine atoms are held in combination with 1 carbon atom, hence the valence of carbon is 4. The formulas of these compounds may be used to illustrate valence as follows:

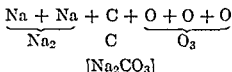


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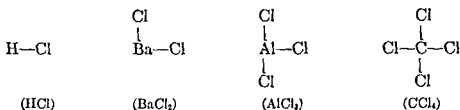
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VALENCE

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positive valence or holding bond, as $\overset{+}{\text{Na}}$, $\overset{++}{\text{Ba}}$, and $\overset{+++}{\text{Al}}$. The negative elements are likewise marked with a - sign for valences, as

$\overset{-}{\text{Cl}}$, $\overset{-}{\text{O}}$, and $\overset{-}{\text{S}}$. A knowledge of the valence of elements is essential in writing the formula of a compound.

Some elements have more than one valence in different compounds. A study of the Periodic Table in the Appendix will confirm the multivalent nature of many elements. In general, the valence of an element is related to the group number and as this group number increases, an element exhibits several valences in its various compounds. In writing the formulas of compounds likely encountered in medicine, a study of the valences of mercury, copper, and iron will be sufficient. Mercury, for example, has a valence of 1 in part of its compounds and 2 in the rest. Copper can also have a valence of 1 or 2. Iron has a valence of 2 in FeCl_2 and 3 in FeCl_3 . In all cases where an element has more than one valence, the lower valence form is given the *ending -ous* and the higher valence form the *ending -ic*. The compound FeCl_2 is called ferrous chloride, while FeCl_3 is ferric chloride.

RADICALS

In many chemical compounds we find groups of elements that act very much like a single element. In chemical reactions, these groups move from one compound to another without the individual elements separating from each other. Such groups of elements as the hydroxyl (OH) group in bases, the nitrate group (NO_3) in nitric acid, the sulfate group (SO_4) in sulfuric acid, and the ammonium group (NH_4) in ammonium compounds are called *radicals*. Compounds containing radicals are written with the radical elements grouped together as Na-OH for sodium hydroxide, $\text{NH}_4\text{-Cl}$ for ammonium chloride and Ca-CO_3 for calcium carbonate.

Each radical has its own valence and if a radical is to be taken more than once in a formula, we enclose the group in parentheses and follow it by the proper subscript.

Barium hydroxide	Ammonium sulfate	Calcium nitrate
$\text{Ba} + \text{OH} + \text{OH}$	$\text{NH}_4 + \text{NH}_4 + \text{SO}_4$	$\text{Ca} + \text{NO}_3 + \text{NO}_3$
$\text{Ba}(\text{OH})_2$	$(\text{NH}_4)_2\text{SO}_4$	$\text{Ca}(\text{NO}_3)_2$

The list of valences of some of the common elements and radicals on page 31 will be found useful in writing the formulas for compounds:

VALENCES OF SOME COMMON ELEMENTS AND RADICALS

Valence of 1:

Positive		Negative	
$\overset{+}{\text{H}}$	hydrogen	$\bar{\text{Cl}}$	chloride
$\overset{+}{\text{Na}}$	sodium	$\bar{\text{OH}}$	hydroxide
$\overset{+}{\text{K}}$	potassium	$\bar{\text{NO}}_2$	nitrite
$\overset{+}{\text{Ag}}$	silver	$\bar{\text{NO}}_3$	nitrate
$\overset{+}{\text{Cu}}$	copper (cuprous)	$\bar{\text{Br}}$	bromide
$\overset{+}{\text{NH}}_4$	ammonium	$\bar{\text{I}}$	iodide
$\overset{+}{\text{Hg}}$	mercury (mercurous)	$\bar{\text{HCO}}_3$	bicarbonate

Valence of 2:

$\overset{++}{\text{Ca}}$	calcium	$\bar{\bar{\text{O}}}$	oxide
$\overset{++}{\text{Cu}}$	copper (cupric)	$\bar{\bar{\text{S}}}$	sulfide
$\overset{++}{\text{Ba}}$	barium	$\bar{\bar{\text{SO}}}_3$	sulfite
$\overset{++}{\text{Hg}}$	mercury (mercuric)	$\bar{\bar{\text{SO}}}_4$	sulfate
$\overset{++}{\text{Pb}}$	lead	$\bar{\bar{\text{CO}}}_3$	carbonate
$\overset{++}{\text{Zn}}$	zinc		
$\overset{++}{\text{Mg}}$	magnesium		
$\overset{++}{\text{Fe}}$	iron (ferrous)		

Valence of 3:

$\overset{+++}{\text{Al}}$	aluminum	$\bar{\bar{\bar{\text{P}}}}\text{O}_4$	phosphate
$\overset{+++}{\text{Fe}}$	iron (ferric)		

Application of Valence

Before we attempt to apply the information in the table to the writing of formulas, it may be of help to state two funda-

mental rules. Since compounds are made up of electrically neutral molecules, *the sum of the valence charges of the positive elements or radicals must equal the sum of the valence charges of the negative elements or radicals.* In the formula for a compound, *the element or radical with a positive valence is always written first.*

When the positive element or radical has the same number of positive charges as the negative element or radical has negative

charges, the formula is easy to write, as: $\overset{+}{\text{H}}\overset{-}{\text{Cl}}$; $\overset{++}{\text{Ba}}\overset{--}{\text{S}}$; $\overset{+++}{\text{Al}}\overset{---}{\text{PO}_4}$.

When a chemical formula is written incorrectly so that the positive and negative valences are not the same, it becomes a simple problem in arithmetic to make the charges balance. To write the formula for barium chloride, we may have begun by

using one of each atom, $\overset{++}{\text{Ba}}\overset{-}{\text{Cl}}$. But to balance the charges, it will take 2 atoms of $\overset{-}{\text{Cl}}$ (2 negative charges) to combine with 1 atom of $\overset{++}{\text{Ba}}$ (2 positive charges) giving $\overset{++}{\text{Ba}}\overset{--}{\text{Cl}_2}$ as the correct formula.

Aluminum hydroxide would be written $\overset{+++}{\text{Al}}(\overset{-}{\text{OH}})_3$ in order to have 3 negative charges to balance the 3 positive charges. Ferric sulfate would require a little more effort to write correctly. The

formula $\overset{+++}{\text{Fe}}\overset{--}{\text{SO}_4}$ is obviously incorrect as the charges do not balance. Two atoms of iron must combine with 3 sulfate radicals to form an electrically neutral molecule $\text{Fe}_2(\text{SO}_4)_3$. To obtain the

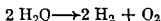
correct formula from $\overset{+++}{\text{Fe}}\overset{--}{\text{SO}_4}$ we determine the least common multiple of the opposite charges. In this case the number would be 6, then divide this number by the number of positive charges (3) to find the correct number of Fe atoms in the formula (2), and by the number of negative charges (2) to find the correct number of SO_4 radicals (3). The correct formula would then be

$\overset{+++}{\text{Fe}_2}(\overset{--}{\text{SO}_4})_3$ which could be checked by multiplying the positive and negative valences by their subscripts to compare the sum of the positive and negative charges. The correct formula for a compound such as calcium phosphate could be determined in a

similar fashion. The positive and negative valences, $\overset{++}{\text{Ca}}\overset{---}{\text{PO}_4}$, would have a least common multiple of 6 giving $\overset{++}{\text{Ca}_3}(\overset{---}{\text{PO}_4})_2$ for the proper formula.

CHEMICAL EQUATIONS

The chemist makes use of symbols and formulas to state the facts of chemical changes or reactions. To represent the electrolysis of water we write the equation for the reaction as follows:



This shorthand form of expression tells us a great deal. At first glance, it merely states that water has been changed into hydrogen and oxygen. More completely, the equation tells us that 2 molecules of water decompose into 2 molecules of hydrogen gas and 1 molecule of oxygen. Quantitatively it states that 2 gram molecular weights of water (2×18.016 gm.) decompose to form 2 gram molecular weights of hydrogen (2×2.016 gm.) and 1 gram molecular weight of oxygen (32 gm.).

Any chemical reaction can be written in the form of an equation if we know the correct formulas for all the substances that react and all the products that are formed.

Balancing Chemical Equations

A chemical equation is significant only if it represents what actually takes place during a chemical reaction. It must signify the actual proportions of the reacting atoms. There are several ways by which we can tell whether an equation is correctly written or "balanced." Since atoms are neither created nor destroyed during a reaction, every atom that reacts must appear in the products of the reaction. Therefore, an equation must have the same number of atoms of each kind on both sides. The simple reaction for the union of iron and sulfur to form iron sulfide may be expressed as follows:



mental rules. Since compounds are made up of electrically neutral molecules, *the sum of the valence charges of the positive elements or radicals must equal the sum of the valence charges of the negative elements or radicals.* In the formula for a compound, *the element or radical with a positive valence is always written first.*

When the positive element or radical has the same number of positive charges as the negative element or radical has negative charges, the formula is easy to write, as: $\overset{+}{\text{H}}\overset{-}{\text{Cl}}$; $\overset{++}{\text{Ba}}\overset{-}{\text{S}}$; $\overset{+++}{\text{Al}}\overset{---}{\text{PO}_4}$.

When a chemical formula is written incorrectly so that the positive and negative valences are not the same, it becomes a simple problem in arithmetic to make the charges balance. To write the formula for barium chloride, we may have begun by using one of each atom, $\overset{++}{\text{Ba}}\overset{-}{\text{Cl}}$. But to balance the charges, it will take 2 atoms of $\overset{-}{\text{Cl}}$ (2 negative charges) to combine with 1 atom of $\overset{++}{\text{Ba}}$ (2 positive charges) giving $\overset{++}{\text{Ba}}\overset{-}{\text{Cl}_2}$ as the correct formula.

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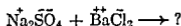
formula $\overset{+++}{\text{Fe}}\overset{--}{\text{SO}_4}$ is obviously incorrect as the charges do not balance. Two atoms of iron must combine with 3 sulfate radicals to form an electrically neutral molecule $\text{Fe}_2(\text{SO}_4)_3$. To obtain the

correct formula from $\overset{+++}{\text{Fe}}\overset{--}{\text{SO}_4}$ we determine the least common multiple of the opposite charges. In this case the number would be 6, then divide this number by the number of positive charges (3) to find the correct number of Fe atoms in the formula (2), and by the number of negative charges (2) to find the correct number of SO_4 radicals (3). The correct formula would then be

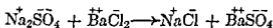
$\overset{+++}{\text{Fe}_2}(\overset{--}{\text{SO}_4})_3$ which could be checked by multiplying the positive and negative valences by their subscripts to compare the sum of the positive and negative charges. The correct formula for a compound such as calcium phosphate could be determined in a

The 2 PO_4 radicals on the left side would balance the 2 on the right side. A recheck would reveal the same number of atoms and radicals of the same kind on each side of the equation; therefore it would be balanced.

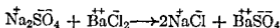
When two compounds react to form two new compounds we are often able to predict the nature of the products that are formed. For example if sodium sulfate were to react with barium chloride what new compounds would we expect to be formed?



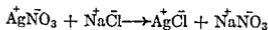
This common type of reaction is called a "double decomposition" or "exchange of partners" equation. Since a reaction occurs and since every compound consists of an element or radical with a positive valence combined with an element or radical with a negative valence, there is only one possible combination of products that can be formed. The Na^+ must combine with the $\bar{\text{Cl}}$ to form the new compound NaCl leaving $\bar{\text{Ba}}^+$ to combine with $\bar{\text{S}}\bar{\text{O}}_4$ to form BaSO_4 as shown below.



A little effort will show that 2 molecules of NaCl must be formed to balance the equation.



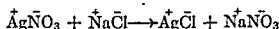
Applying this same principle to the equation for the reaction between silver nitrate and sodium chloride, we may reason as follows:



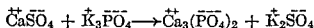
The Ag^+ must find a new partner with a negative valence in order to form a silver salt other than AgNO_3 . It therefore combines with $\bar{\text{Cl}}$ leaving Na^+ and $\bar{\text{N}}\bar{\text{O}}_3$ to form NaNO_3 . In other words, the Ag^+ and Na^+ merely exchange partners to form two entirely new

If we check the numbers of each kind of atom, we find that there are the same number of atoms of each kind on each side of the equation, which means that it is *balanced*.

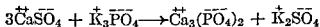
Since there are a great many chemical reactions that involve two compounds it may be well to consider the equations for such reactions. When a silver nitrate solution is added to a solution that contains sodium chloride, the two salts react to form insoluble silver chloride and sodium nitrate.



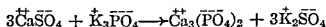
Inspection of both sides of the equation will reveal that the equation is balanced. In a study of equations it will be found very helpful to write the valence charges of each atom or radical in a compound above the symbols. This practice will aid in writing correct formulas for the compounds and in balancing the equations. An example of a more difficult equation to balance would be represented by the reaction of calcium sulfate and potassium phosphate to form calcium phosphate and potassium sulfate. We could start by writing the correct formulas for the compounds involved.



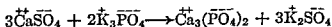
To balance the equation we begin by comparing the number of Ca atoms on both sides. Since there are 3 on the right and 1 on the left we must take 3 molecules of CaSO_4 to furnish 3 Ca atoms, thus



Comparing next the SO_4 radicals on each side, it will be found necessary to take 3 molecules of K_2SO_4 to balance the 3 SO_4 radicals on the left side.



The next step would involve the K atoms. By taking 2 molecules of K_3PO_4 on the left we would have 6 atoms of K on each side.



4. How many atoms of each kind are there in the formula $K_2Cr_2O_7$?
5. In what way is the element hydrogen useful in determining the valence of other elements?
6. Which type of elements usually have positive valence and which have negative valence?
7. Name three elements that have two valences, giving the valence in each case.
8. From the list of valences of common elements and radicals, pick out the radicals and give their valence.
9. What two fundamental rules are useful in writing formulas?
10. Write the correct formulas for the compounds that would result from the proper combination of the following pairs of elements:

Al and Cl	NH_4 and SO_4
Ba and OH	Fe and O (ferric Fe)
Ca and SO_4	Hg and Cl (mercuric Hg)
11. In writing a chemical equation, what three steps should be followed?
12. What should never be done in balancing a chemical equation?
13. If an equation will not balance, what should be checked first?
14. In writing most chemical equations, how can you predict the products of the reaction?
15. Write and balance the equations for the following reactions:
 - (a) Aluminum chloride reacts with sodium hydroxide to form?
 - (b) Potassium metal reacts with water to form potassium hydroxide and hydrogen gas.
 - (c) Calcium chloride and sodium sulfate react to form?
 - (d) Aluminum sulfate and potassium hydroxide react to form?

compounds. Similar reasoning may be applied to the majority of chemical reactions.

We may summarize equation writing as follows:

1. Write the correct formulas for the substances that are reacting by combining the symbols for the elements or radicals in each compound, then balancing the valence charges.
2. If possible, determine the products that are formed and write their correct formulas.
3. Balance the equation so that you have the same number of atoms of each kind on both sides.

In equation writing, it cannot be stressed too strongly that you can never change a formula to make the atoms balance. *If the formulas are written correctly, the equation can always be balanced.* When a given equation cannot be balanced, you should check the formulas to see if they are correct.

It is well to *practice writing formulas* until you thoroughly understand how the figures in the formulas and preceding the formulas apply to the different atoms. For examples, BaCO_3 indicates 1 atom of barium, 1 atom of carbon and 3 atoms of oxygen; $\text{Ca}(\text{NO}_3)_2$, 1 atom of calcium, 2 atoms of nitrogen, and 6 (2×3) atoms of oxygen; and $\text{Al}_2(\text{SO}_4)_3$, 2 atoms of aluminum, 3 atoms of sulfur, and 12 (3×4) atoms of oxygen. When a number precedes the formula as in 2NaCl , it means 2 molecules of sodium chloride; $3 \text{H}_2\text{O}$ means 3 molecules of water; and $4 \text{H}_2\text{CO}_3$, means 4 molecules of carbonic acid. The number that precedes a formula multiplies every atom in it, therefore, $4 \text{H}_2\text{CO}_3$ indicates 8 (4×2) hydrogen atoms, 4 carbon atoms, and 12 (4×3) oxygen atoms; and $2 \text{Al}_2(\text{SO}_4)_3$ indicates 4 (2×2) aluminum atoms, 6 (2×3) sulfur atoms and 24 ($2 \times 3 \times 4$) oxygen atoms.

REVIEW QUESTIONS

1. Why are the symbols for the elements often called atomic symbols?
2. The phosphoric acid molecule contains 3 atoms of hydrogen, 1 atom of phosphorus, and 4 atoms of oxygen. Write the formula for phosphoric acid.
3. Explain the different meanings of the following terms: 3N , N_2 , and 4N_2 .

4. How many atoms of each kind are there in the formula $K_2Cr_2O_7$?
5. In what way is the element hydrogen useful in determining the valence of other elements?
6. Which type of elements usually have positive valence and which have negative valence?
7. Name three elements that have two valences, giving the valence in each case.
8. From the list of valences of common elements and radicals, pick out the radicals and give their valence
9. What two fundamental rules are useful in writing formulas?
10. Write the correct formulas for the compounds that would result from the proper combination of the following pairs of elements.

Al and Cl	NH_4 and SO_4
Ba and OH	Fe and O (ferric Fe)
Ca and SO_4	Hg and Cl (mercuric Hg)
11. In writing a chemical equation, what three steps should be followed?
12. What should never be done in balancing a chemical equation?
13. If an equation will not balance, what should be checked first?
14. In writing most chemical equations, how can you predict the products of the reaction?
15. Write and balance the equations for the following reactions:
 - (a) Aluminum chloride reacts with sodium hydroxide to form?
 - (b) Potassium metal reacts with water to form potassium hydroxide and hydrogen gas.
 - (c) Calcium chloride and sodium sulfate react to form?
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CHAPTER V

Oxygen, Oxidation and Reduction

OXYGEN, the most abundant and probably the most important of all the elements, is essential to our continued existence. Without oxygen, it would be impossible to live for more than a few minutes, whereas you might live for a month or more without food, and for several days without water. All plants and animals except certain bacteria are dependent upon oxygen to maintain life. Even fish that live in water must have a supply of oxygen. The fish would smother if the water were boiled until all of the dissolved oxygen was driven out.

Oxygen is essential for many processes other than the maintenance of life. Without it, we could have no fire to heat our homes, cook our food, or make possible our many industrial processes. The treatment of certain diseases, the purification of drinking water, and the disposal of sewage are dependent on an abundant supply of oxygen.

OCCURRENCE

Of all the elements in the earth's surface, oxygen is the most abundant. One-fifth of the volume of the air, eight-ninths by weight of water, and approximately one-half of the earth's crust is oxygen. In the air it exists as free molecular oxygen (O_2), elsewhere it is found combined with many other elements in the form of oxides. Oxygen is an important constituent of the major food-stuffs—carbohydrates, fats, and proteins—and makes up about two-thirds of the human body.

PREPARATION

Oxygen is usually prepared commercially from air, which is essentially a mixture of this element and nitrogen. Air is liquefied by subjecting it to a high pressure at a low temperature. When the liquid air is allowed to evaporate, the more volatile nitrogen escapes first, leaving behind the fairly pure oxygen. The oxygen gas is then forced into steel cylinders under high pressure and stored for future use.

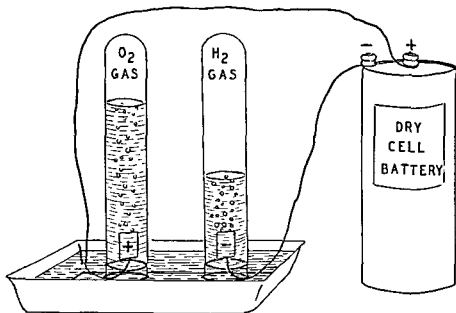
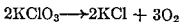


Fig. 9. A simple illustration of the electrolysis of water.

Another commercial source of pure oxygen is the electrolysis of water. When an electric current is passed through water, oxygen forms at the positive pole, or anode, and hydrogen forms at the negative pole, or cathode (Fig. 9). The oxygen and hydrogen gas thus formed are drawn off and stored under pressure.

In the laboratory, oxygen is usually prepared by heating potassium chlorate. The reaction may be represented as follows:



This formation of oxygen proceeds slowly when a test tube con-

taining potassium chlorate is heated by the flame of a bunsen burner. If some manganese dioxide (MnO_2) is mixed with the potassium chlorate before heating, the rate of formation of oxygen is increased considerably. Experimentally, it can be shown that the manganese dioxide is not changed in the reaction and can be recovered from the tube. A substance of this kind that can influence the speed of a chemical reaction without being altered itself is called a *catalyst*. The success of many commercial processes depends upon the finding of a proper catalyst; also, the

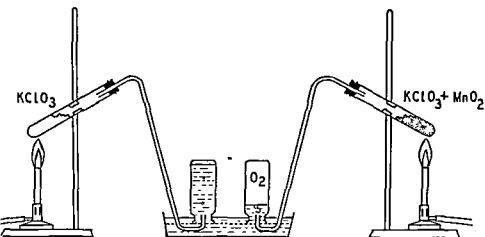


Fig. 10 Catalytic action. When the tubes are heated under identical temperature conditions, the tube containing the catalyst liberates oxygen rapidly, whereas the tube containing potassium chlorate alone, liberates practically no oxygen.

majority of the chemical reactions that occur in our bodies are controlled by catalysts.

A visual illustration of the effect of the catalyst, manganese dioxide, is shown in Fig. 10.

PROPERTIES

Oxygen is a transparent, colorless, tasteless, and odorless gas. It is slightly heavier than air and sparingly soluble in water. Approximately 3 cc. of oxygen will dissolve in 100 cc. of water at ordinary temperatures. This slight solubility insures a supply of the gas to aquatic plants and animals, and for the conversion

of sewage and other contaminating substances in natural water into harmless material.

The outstanding chemical property of oxygen is its ability to form compounds with nearly all known elements. These com-



Fig. 11. The rusting of iron and the decay of wood are both examples of oxygenation. (From Brauer, O. L., *Chemistry and Its Wonders*. New York, American Book Company.)

pounds of oxygen with metals or nonmetals are called *oxides*. The union of a substance with oxygen may be called *oxygenation*. The burning of wood, the rusting of iron, and the decay of plant and animal matter are examples of oxygenation. Oxygen is able to unite with food and tissue substances in the body at rela-

tively low temperatures because these reactions are hastened by catalysts, called *enzymes*.

COMBUSTION

When a substance unites with oxygen so rapidly that heat and light are produced in the reaction, we say the substance is burning. We commonly speak of rapid oxidation, or burning, as *combustion* although combustion may occur in the absence of oxygen.

Substances that will burn readily, such as paper, wood, candle, illuminating gas, and gasoline, are called *combustible*; those that will not burn, such as asbestos, stone, and clay, are called *incombustible*. Since air is only one-fifth oxygen, substances burn less vigorously in it than in the pure gas, and many substances which are incombustible in air burn in oxygen. For example, powdered sulfur burns feebly in air but blazes up vigorously when thrust into oxygen, while iron wire is incombustible in air, yet burns brightly in the pure gas. It is often said that a substance is "burned" in the body to give energy. This merely means that the substance unites with oxygen in the tissues. Although burning commonly occurs with oxygen as one of the reacting substances, it can occur in the absence of this element. Hydrogen will "burn" in the presence of chlorine to form hydrogen chloride. If you sprinkle powdered antimony into chlorine gas, "burning" will start at ordinary temperatures.

SPONTANEOUS COMBUSTION

When a substance unites slowly with oxygen, heat is produced in the reaction. If the heat cannot escape, the temperature of the substance gradually rises, thus increasing the rate of oxygenation. If the process is allowed to continue, the temperature is raised to a point at which the material bursts into flame. This temperature is called the *kindling temperature* and the process which causes the material to burst into flame is called *spontaneous combustion*. A burning match will set fire to a great many combustible substances because the reaction between the wood of the match and the oxygen of the air produces sufficient heat

to raise the temperature of these substances to their kindling temperature. Substances with a low kindling temperature, as illuminating gas, ether, and gasoline, must be handled with care to prevent them from becoming fire hazards. Damp hay in a farmer's barn and oily rags left by painters often catch fire by spontaneous combustion.

EXTINGUISHING FIRES

There are two common ways to put out a fire: (1) by removing the source of oxygen from the burning material; (2) by lowering the temperature of the burning substance to below its

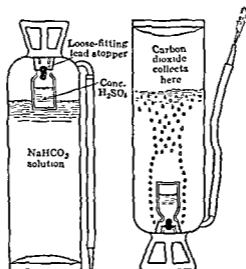
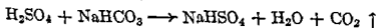


Fig. 12. A common type of fire extinguisher. (From Deming, H. G.: General Chemistry. New York, John Wiley & Sons, Inc.)

kindling temperature. Chemical fire extinguishers contain a liquid which cools the burning substances below its kindling temperature and surrounds it with an incombustible gas. A common type of extinguisher contains water and chemicals that react to form carbon dioxide (CO_2) gas. In Fig. 12, when the cylinder is inverted, the acid is poured into the sodium bicarbonate solution, forming carbon dioxide gas as shown in the reaction:



This gas is heavier than air and settles over the burning material, excluding its oxygen supply. Another common extinguisher uses a heavy, incombustible liquid called carbon tetrachloride. When the liquid is sprayed on a fire, it forms a blanket of incombustible gas over the burning substances, thus removing the oxygen supply. Carbon tetrachloride extinguishers should not be used in closed quarters because of the toxicity of the vapors. There is also the possibility that poison gases such as phosgene may be formed in the use of these extinguishers. One of the best extinguishers for use in the chemical laboratory consists of a cylinder of carbon dioxide gas connected by a hose to a long, funnel-

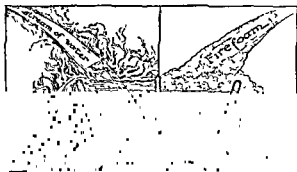


Fig. 13. The use of foamite in extinguishing oil fires. Left, the result of pouring water on an oil fire. Right, the action of foamite. (From Brauer, O. L. : Chemistry and Its Wonders. New York, American Book Company.)

shaped nozzle for directing the gas at the base of a flame. All three of the extinguishers just mentioned are shown in Fig.14 on the left. The carbon tetrachloride type are the small cylinders just above the common sodium bicarbonate solution type, while on the extreme left is a cylinder of carbon dioxide gas connected to a spraying nozzle.

Oil or gasoline fires cannot be extinguished with water because these liquids are lighter than water and will float on the surface, thus spreading the fire. The water layer underneath the burning oil is unable to lower the temperature below the kindling temperature. An effective fire extinguisher for gasoline or oil fires contains foamite, a mixture of chemicals and licorice, which

forms a thick foam of carbon dioxide bubbles on the surface of the burning oil and thus removes the oxygen.

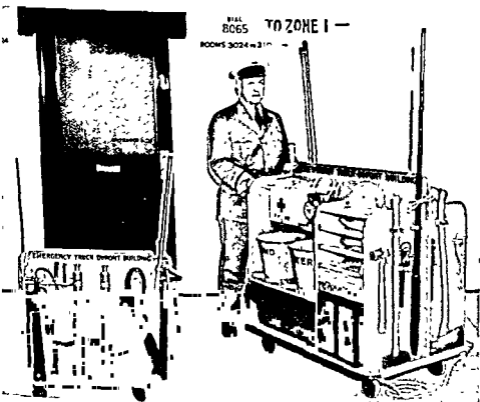


Fig. 14. A "Fire Buggy." A recent development in portable fire-fighting equipment for use in hospitals. (Courtesy of The duPont Magazine.)

USES OF OXYGEN

In Therapy

When oxygen is breathed into the lungs, it diffuses into the blood and loosely combines with the *hemoglobin* (red pigment of the blood). This unstable compound of oxygen and hemoglobin is called *oxyhemoglobin* and is responsible for the bright red color of arterial blood. The oxyhemoglobin is carried to the tissues where it releases its oxygen to react with food and waste products in the tissue cells. One of the waste products formed is carbon dioxide gas, which is carried back to the lungs and exhaled. When the oxyhemoglobin loses its oxygen, it changes from a bright red

to deep purple color which accounts for the color of venous blood.

If the oxygen concentration in the air is diminished, it is often necessary to supply an additional source of the gas. Aviators flying at high altitudes, sailors in submarines, and men engaged in mine and fire rescue work find it necessary to carry oxygen for breathing. A person who has been exposed to smoke



Fig. 15. The administration of a mixture of nitrous oxide and oxygen to produce anesthesia. (From Cole, W. H., and Elman, R.: Textbook of General Surgery. New York, Appleton-Century-Crofts, Inc.)

or gases other than oxygen, to oxygen-low atmospheres, or who has been under water for several minutes, usually becomes unconscious from the lack of oxygen. This oxygen lack is called *asphyxiation* and is treated by forcing the patient to breathe pure oxygen in an attempt to bring the oxygen content of the blood up to normal. Asphyxiation is also caused by breathing a gas such as carbon monoxide (CO), which unites with hemoglobin and thus prevents oxygen from combining with the hemo-



Fig. 16. An oxygen tent in use. (Courtesy of Dr. S. C. Cullen, University of Iowa Hospitals.)

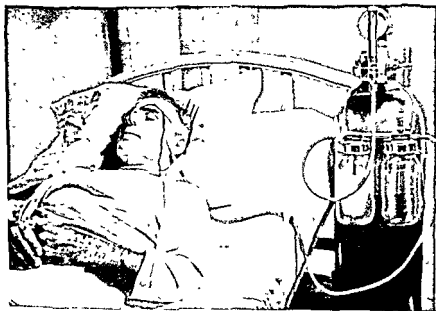


Fig. 17. The administration of oxygen through a nasal catheter. (Courtesy of Dr. S. C. Cullen, University of Iowa Hospitals)

globin. The administration of a high concentration of oxygen is an effective treatment in carbon monoxide poisoning.

In dental surgery, where a gas anesthetic such as nitrous oxide (N_2O , laughing gas) is used, oxygen is mixed with the gas to prevent asphyxiation. Patients suffering from pneumonia and other lung diseases may have their normal lung capacity diminished by fluid to such an extent that they are unable to obtain an

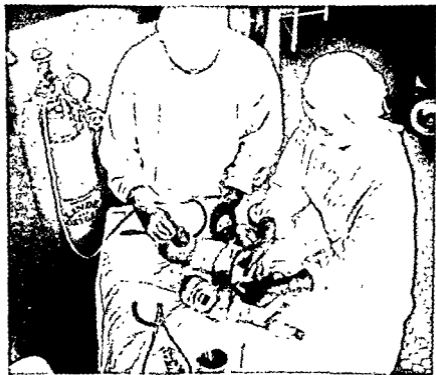


Fig. 18. Oxygen administered to newborn babies. (Courtesy of Dr. S. C. Cullen, University of Iowa Hospitals.)

adequate supply of oxygen from the air. The administration of oxygen may sustain the patient until the diseased lung is healed. Physicians have found that newborn babies who at birth experience difficulty in breathing or whose lungs do not readily expand can often be revived by a mixture of oxygen and a small amount of carbon dioxide. The carbon dioxide acts as a respiratory stimulant.



Fig. 19. The use of an oxyacetylene torch in cutting steel plate. (Courtesy of The Welding Journal)

In Industry

An important industrial use of oxygen is in the production of intense heat for cutting and welding iron and steel plates. When oxygen is mixed with hydrogen or acetylene gas and the mixture is ignited, the heat produced is sufficient to melt steel (Fig. 19). The common type of welding torch uses an oxyacetylene flame.

OXIDATION AND REDUCTION

The union of oxygen with an element always causes an increase in the valence of the element. For example, when metallic

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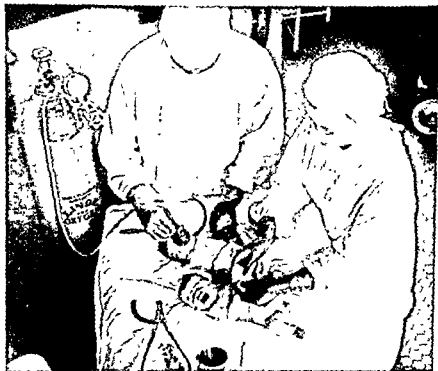
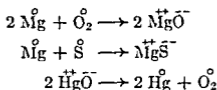


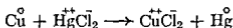
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(Since an element in the free state has zero valence, we can represent this valence by a small zero over the symbol.) In the first reaction, magnesium is oxidized from a valence of 0 to +2 while oxygen is reduced from 0 to -2. This confirms the statement that an oxidation is always accompanied by a reduction and that the oxidation and reduction occur to an equal degree (0 to +2 versus 0 to -2). The second reaction is similar to the first except that oxygen is not involved. In the third reaction, mercury is reduced from a valence of +2 to 0 while oxygen is oxidized from a valence of -2 to 0.

Another type of oxidation-reduction reaction that is often encountered is between a metal and a salt. For example, copper reacts with mercuric chloride to form cupric chloride and metallic mercury:



In this reaction, copper is oxidized from a valence of 0 to +2 while mercury is reduced from +2 to 0. The oxidizing agent is mercuric chloride, since it causes copper to be oxidized. The metallic copper would be the reducing agent because it brings about the reduction of the mercury.

The body requires a constant source of energy to carry on its manifold activities. Energy for muscular movement, for maintenance of body temperature and so on, is obtained from the food by means of oxidation-reduction reactions. It requires a good many of these reactions to convert our meals into enough energy for a day's work.

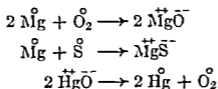
Antiseptic Agents

Many of the common antiseptic agents owe their efficacy to the fact that they are oxidizing agents, since the oxygen destroys bacteria and the food on which they live. Hydrogen peroxide

magnesium combines with oxygen, its valence is increased from 0 to 2. (Uncombined elements such as metals and gases are considered as having no valence, or a valence of zero.) In a similar fashion, the combination of oxygen with a compound always produces a rise in the valence of one or more of the elements in the compound. However, the valence of an element in the free state or in a compound may be increased by combination with elements other than oxygen. In combining the metallic magnesium with sulfur, we form magnesium sulfide (MgS) and again raise the valence of the magnesium from 0 to 2. Whenever the valence of an element is increased in a reaction, the process is called *oxidation*. The element that is oxidized may be in the free or combined form, and its valence may be raised by combination with oxygen or some other element. The agent which causes the oxidation of an element or compound is called an *oxidizing agent*. Simple addition of oxygen to a substance always results in an oxidation reaction; there are also many oxidation reactions which do not involve oxygen and are therefore not oxygenation reactions.

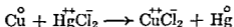
Reduction is the opposite of oxidation and is the process in which the valence of an element is decreased. Many reduction reactions also involve a loss of oxygen from a compound. For example, if we decomposed mercuric oxide by heating, we would form oxygen and metallic mercury. The mercury has been reduced in the reaction as its valence decreased from $+2$ to 0 and it lost oxygen. In the reaction between magnesium and sulfur to form magnesium sulfide, the valence of the sulfur was decreased from 0 to -2 indicating that the sulfur had been reduced. The agent which causes the reduction of an element is known as a *reducing agent*.

We commonly speak of *oxidation-reduction reactions* rather than separate oxidation or reduction reactions. *In any reaction where an oxidation occurs, it is always accompanied by a reduction, and the oxidation and reduction always take place to an equal degree.* We can write the oxidation-reduction reactions we have already discussed as follows:



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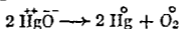
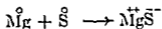
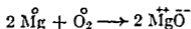
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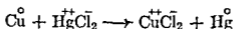
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(H_2O_2) in a 3 per cent solution is a mild oxidizing agent and was once extensively used as an antiseptic. In contact with a wound, it effervesces and releases oxygen bubbles which aid in cleansing the wound. It also exerts a mild antiseptic action. Potassium permanganate (KMnO_4) is an antiseptic that releases oxygen when in contact with organic matter. In dilute solutions, it is effective in treating infections of the urethra and bladder. Iodine, in solution, is widely used as an antiseptic for minor cuts and wounds and for application to the skin in preparation for surgical procedures.

Stain Removal

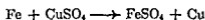
The pigment of certain dyestuffs and stains is converted to a colorless compound by oxidation, while other pigments are decolorized by reduction. Therefore, bleaching agents usually consist of an oxidizing or a reducing agent and often have antiseptic properties. Hydrogen peroxide is used to remove blood stains from linen and to bleach organic matter such as hair, silk, and feathers. Potassium permanganate will remove stains from almost all white fabrics but should not be used on rayon. After the stain has been oxidized, the permanganate can be removed by an acid solution of hydrogen peroxide or by oxalic acid. A common bleaching solution is Javelle water, which is a solution of sodium hypochlorite. Hilex, chlorox, and many other household bleaching preparations contain sodium hypochlorite. It is very effective for removing the majority of the stains from cotton or linen encountered in the nursery and home.

Oxalic acid (COOH)₂ is a reducing agent that is used to remove iron stains, ink stains, and especially potassium permanganate stains. Another reducing agent that is useful is sodium thiosulfate ($\text{Na}_2\text{S}_2\text{O}_3$). It is very effective in removing iodine stains and is also used to remove stains caused by compounds that contain silver.

REVIEW QUESTIONS

1. Describe two methods for the preparation of oxygen.
2. What is a catalyst? What catalyst is used in the laboratory preparation of oxygen?

3. Why do substances burn more rapidly in oxygen than in air?
4. What conditions are necessary to cause *spontaneous combustion*?
5. Explain the two fundamental principles that are applied in extinguishing a fire.
6. Why are the majority of fires extinguished with water?
7. List several instances where an additional source of oxygen is necessary for normal respiration.
8. Why are small amounts of carbon dioxide often administered with oxygen in oxygen therapy?
9. How is oxygen carried from the lungs to the various tissues of the body?
10. Define oxidation and reduction.
11. What is an oxidizing agent; a reducing agent? Give examples of each.
12. Why do we always speak of an oxidation-reduction reaction rather than a separate oxidation or reduction reaction?
13. In the following oxidation-reduction reaction:



What is oxidized? What is reduced? What is the oxidizing agent, the reducing agent?

14. Many of the common antiseptics are either oxidizing or reducing agents. How does this explain their antiseptic action?
15. Bleaching agents and stain removers are effective because they either oxidize or reduce dyestuffs or stains. Name two that are oxidizing agents and two that are reducing agents. List the stains that each of the four will remove

CHAPTER VI

Water

WATER is without a doubt the most common and the most important liquid in the world. As a substance essential to our existence, it ranks next to oxygen in importance. The body can survive for several weeks without food but for only a few days without water. The digestion of food, the circulation, the elimination of waste, the regulation of body temperature, and many other vital functions depend upon an adequate supply of water. Plants also must have water, and the crops that help make up the nation's food supply are dependent on proper rainfall or irrigation.

OCCURRENCE

Water is the most abundant of all chemical compounds. About three-fourths of the surface of the earth is covered with water, either as a liquid or in the arctic regions as ice. The soil contains large quantities of water which is essential for the growth of plants. Its presence in the atmosphere is readily recognized, because it often condenses into dew, fog, rain, or snow. Approximately two-thirds of the body weight is water, while most of the foods we eat have a water content of from 10 to 90 per cent. Bread, for example, is about 35 per cent, meat about 70 per cent, and most vegetables are over 75 per cent water.

PHYSICAL PROPERTIES

Pure water has no odor, taste, or color. The blue or green color of lakes and oceans is due to the presence of finely divided solid material. Water freezes at 0°C . (32°F .) and boils at 100°C . (212°F .)

When water freezes, it expands rapidly, increasing its volume by nearly one-tenth in changing from water to ice. This property of expansion on freezing explains why pipes and other vessels containing water burst upon freezing. Since ice is lighter than water, the surface of a river or lake freezes first and the layer of ice protects the aquatic plants and animals from the cold.

As the temperature of water is raised, it vaporizes more and more rapidly until it reaches the boiling point. The temperature remains constant during the boiling process and the vapor or steam given off is a colorless gas which condenses into a cloud of visible water particles in the cold air. The boiling point is 100°C . at sea level (an atmospheric pressure of 760 mm.). On high mountains, the atmospheric pressure is lower, causing a lowering in the boiling point. Cooking food at high altitudes may be difficult because the water boils before the temperature is high enough for cooking. This difficulty may be overcome by the use of a pressure cooker, where the steam that is formed in boiling is confined in a vessel to increase the pressure. The temperature may then be raised above the boiling point of water. For instance, a steam pressure of 15 pounds will raise the internal temperature about 20°C . above the boiling point of water. The increased temperature that can be obtained in a pressure cooker or in an autoclave is far more efficient than boiling water in cooking or in sterilization.

One of the most remarkable properties of water is its ability to dissolve other substances. It is more nearly a "universal solvent" than any liquid known. In the laboratory, the majority of chemical reactions will not take place unless the substances are in solution in water. In the living organism, the constituents of the cells are kept in solution by water and most of the reactions that take place in the tissues will not take place in its absence.

The universal distribution of water and its widespread use in the laboratory have caused many measurements to be based on its physical properties. For instance, the centigrade thermometer was based on the freezing and boiling points of water. The position of the mercury at the freezing point was marked as 0°C . and at the boiling point as 100°C . The length of the mercury

CHAPTER VI

Water

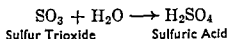
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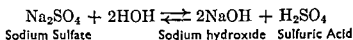
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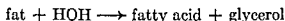
An *acid* is a compound that contains hydrogen in a chemically reactive form.

One of the most important chemical properties of water is concerned with the process of hydrolysis. In *hydrolysis*, or breaking apart with water, the compounds are split into two parts, the hydrogen of the water uniting with one part to make an acid and the hydroxyl uniting with the other to make a hydroxide. An example of hydrolysis would be the reaction of water and a compound like sodium sulfate.



The double arrow indicates that the reaction can go in both directions. Actually only a small amount of the sodium sulfate reacts with water in this way.

The process of digestion in the body is mainly one of hydrolysis. For example, a complex molecule like fat is hydrolyzed as follows:



The H of water goes into the fatty acid while the OH is an integral part of the glycerol molecule. Many examples of hydrolysis will be discussed later in the study of the chemistry of the reactions that occur in the body.

HYDRATES

Water molecules combine with the molecules of certain substances, forming loose chemical combinations called *hydrates*. These hydrates form well-defined crystals when their solutions are allowed to evaporate slowly. For example, copper sulfate forms blue crystals when a solution of this substance evaporates slowly. The formula for crystalline copper sulfate is $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$. The water held in combination is called *water of crystallization* and is written separately to indicate its loose chemical attachment. When this hydrate is heated, it loses its water of crystal-

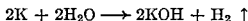
column between these two marks was divided into 100 equal divisions called degrees. The name centigrade comes from the 100 divisions between these points.

The specific gravity of a substance is compared to water as a standard. The density of a liquid is called its *specific gravity* and is expressed as weight (in grams) per unit of volume (in cubic centimeters). The specific gravity of water is 1.000, since 1 cc. of water at 4° C. weighs 1.000 gm. If a specimen of urine weighed 1.030 gm. per cc. (gram per cubic centimeter) it would have a specific gravity of 1.030, and 1 cc. of the urine would be 1.030 times as heavy as 1 cc. of water.

CHEMICAL PROPERTIES

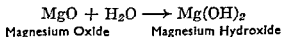
Water is one of the most stable compounds known, and for many years it was thought to be an element. It may be heated to very high temperatures (2000° C.) without appreciable decomposition. However, if an electric current is passed through it, decomposition occurs; 2 volumes of hydrogen are produced for each volume of oxygen. The oxygen atom is approximately 16 times as heavy as the hydrogen atom, so that water is, by weight, eight-ninths oxygen and one-ninth hydrogen.

Another interesting chemical property of water is its action with certain metals. If a small piece of metallic potassium is placed in water, a violent reaction takes place with the formation of a hydroxide (compounds that contain the OH radical) and hydrogen gas:



The compound that is formed is called potassium hydroxide. Hydrogen gas, like oxygen, exists as molecules, each containing 2 hydrogen atoms. (The small vertical arrow pointing upward, written after H_2 indicates that this product is a gas.)

Water will combine with the oxides of some metals to form a metallic hydroxide, which is also called a *base*.

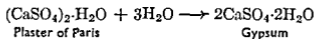


Certain oxides of nonmetals react with water to form acids.

lization and changes into a white powder whose formula is CuSO_4 . Examples of other common hydrates are washing soda, $\text{Na}_2\text{CO}_3 \cdot 10\text{H}_2\text{O}$; alum, $\text{K}_2\text{Al}_2(\text{SO}_4)_4 \cdot 24\text{H}_2\text{O}$; gypsum, $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$; and crystalline sodium sulfate, $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$.

When the water of crystallization has been removed from a hydrate, the resulting compound is said to be *anhydrous*. Substances which give up water of crystallization on exposure to air at ordinary temperatures are called *efflorescent*. Other substances take up water on exposure to atmospheric conditions and are said to be *hygroscopic*. If they take up so much water from the air that they finally dissolve in it, they are called *deliquescent* substances. Compounds like sodium hydroxide and calcium chloride are so deliquescent that they take up water from other materials. Calcium chloride is commonly used as a drying agent or desiccating agent by the chemist. It is also used on dirt roads to keep down the dust, because of its ability to take up water from the atmosphere.

A hydrate of special interest is gypsum, or calcium sulfate ($\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$), which on heating gives up part of its water to form plaster of paris, $(\text{CaSO}_4)_2 \cdot \text{H}_2\text{O}$. When the plaster of paris is mixed with water it "sets" in a few minutes to reform hard crystalline gypsum. In setting, it expands slightly to form a tight cast or mold. Plaster of paris is used extensively in making surgical casts, an example of which is shown in Fig. 20. Chemically, the reaction may be represented as follows:



DEHYDRATION

When water is removed from a substance, the process is called *dehydration*. Food may be preserved by drying because the bacteria and other micro-organisms that spoil food must have water in order to live. Dehydration of food became a very important process during the Second World War. The great decrease in the weight and bulk of dehydrated foods was an important factor in the transportation of supplies to the battlefront and to

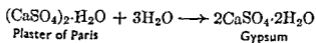


Fig. 20. A walking cast for a fracture of the heel bone. (From Geckeler, E. O.: *Plaster of Paris Technic*, Baltimore, The Williams and Wilkins Co.)

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our allies. A relatively small box of dehydrated foodstuff would feed five men for a day. This was a very definite advantage under battle conditions when supply lines were difficult to maintain or when supplies had to be dropped from the air into inaccessible regions.

PURIFICATION OF WATER

Naturally occurring water contains impurities dissolved from the rocks and soil. Even rain water contains particles of dust and dissolved gases from the air. The impurities present in water may be classified as either mineral or organic matter.

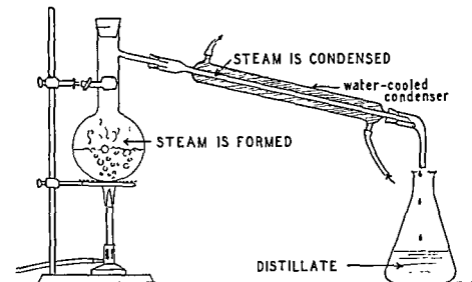


Fig. 21. A simple apparatus for the distillation of water.

The mineral matter found in natural water usually consists of common salt and various compounds of calcium, magnesium, and iron. Water that contains these dissolved salts does not readily form a lather with soap and is called *hard water*, while water with little or no mineral matter lathers easily and is called *soft water*.

The organic matter in water is derived from decaying animal and vegetable material. Bacteria utilize this type of material for food, and may cause diseases unless they are removed before the water is used for drinking purposes.

A source of pure drinking water is extremely important to the health of a community. For this reason, it would be appropriate to consider several of the methods for the purification of water.

Distillation

In the process of distillation, water is boiled and the resulting steam is cooled and condensed in a different container, as illustrated in Fig. 21. The condensed steam is called the distillate, or distilled water. The chemist uses this method to produce water free from bacteria and dissolved mineral matter. Distilled water is used widely in the preparation of solutions in the laboratory and in the hospital. Distillation is the most effective method for the purification of water, but is too expensive to be employed by large towns or cities.

Boiling

Water from natural sources may be made safe for drinking by boiling for ten to fifteen minutes. This process does not remove the impurities but does kill any pathogenic bacteria that might be present. The flat taste of boiled water is due to the loss of dissolved gases; it may be improved by aeration, such as pouring water from one vessel to another. This method of water purification is reliable in emergencies but is not generally employed for civilian water supplies.

Filtration

In the laboratory, suspended material is separated from water by passing the liquid through a porous material which has holes that are smaller than the suspended matter, thus holding it back. The dissolved impurities are not removed by this method. On a large scale, as in city water works, the water is filtered through beds of sand (Fig. 22). The bacteria are on the suspended organic matter and are largely removed by filtration. To destroy bacteria completely, it has become general practice to treat the water with chlorine, a substance which kills the remaining micro-organisms.

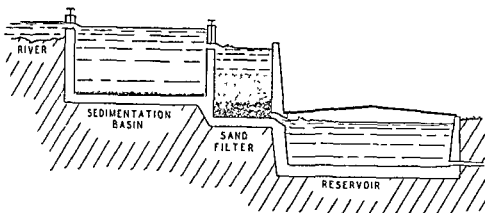


Fig. 22. Filtration as used by large cities in the purification of water.

Aeration

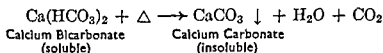
Water may be purified by exposure to air for long periods. The oxygen of the air dissolves in the water and oxidizes organic material, thus depriving bacteria of their source of food. It also kills bacteria by direct chemical reaction. Most cities do not depend on this process alone for water purification but use it to remove objectionable tastes and odors from the water. Aeration of water supplies is usually accomplished by spraying the water into the air from fountains, or by allowing it to flow in thin sheets over tiles.

HARD AND SOFT WATER

Since the common methods of water purification do not remove the dissolved inorganic matter, many cities have hard water. There are many disadvantages to the use of hard water. It requires a large amount of soap to form a lather because the soap forms an insoluble compound or "curd" with the minerals in the water. This curd adheres to clothing and makes it rough and irritable to bedridden patients. Cooking with hard water has a toughening effect on foods, also the iron salts in hard water often discolor white fabrics, pottery, and enamelware. When hard water is boiled, the mineral salts deposit a scale on the sides of boilers, pipes, and utensils in which it is heated. This causes not only a waste of fuel but also a corrosion of the metal as well. Hard water should never be used in a sterilizer of surgical instruments because it dulls the cutting edges.

Methods for Softening Water

The inorganic matter which is present in hard water usually consists of bicarbonates, sulfates, or chlorides of calcium, magnesium, and iron. Water which contains only calcium or magnesium bicarbonate is called *temporary hard water*, because these salts can be removed by heating. When heated they are converted into the insoluble carbonates which form most of the scale on boilers and teakettles. Temporary hard water can therefore be softened by boiling:

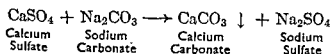


(The small triangle is used by chemists as a symbol for heat, while the small vertical arrow pointing downward after the CaCO_3 indicates the formation of an insoluble substance or precipitate.)

Water which contains sulfates or chlorides of calcium, magnesium, or iron is called *permanent hard water* because it does not lose these salts on heating. Permanent hard water can be softened by adding a chemical compound which will convert the soluble calcium, magnesium, or iron salts into insoluble precipitates which may be removed by filtration. The following compounds are commonly used for water softening:

Sodium carbonate	Na_2CO_3 (washing soda)
Sodium tetraborate	$\text{Na}_2\text{B}_4\text{O}_7$ (borax)
Ammonium hydroxide	NH_4OH (household ammonia)
Trisodium phosphate	Na_3PO_4
Sodium hydroxide...	NaOH (caustic soda or lye)
Mixture of calcium hydroxide, Ca(OH)_2 , and sodium carbonate, Na_2CO_3	

The reaction between a soluble calcium salt and sodium carbonate may be used as a typical water softening reaction



Removal of the insoluble calcium carbonate leaves soft water.

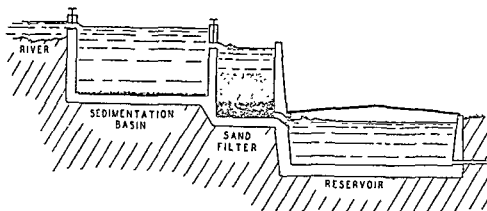


Fig. 22. Filtration as used by large cities in the purification of water.

Aeration

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CHAPTER VII

Solutions

WE HAVE already stated that one of the most important properties of water is its ability to dissolve many other substances. If we dissolve common salt or sugar in water, the resulting mixture is called a solution. The salt or sugar molecules become uniformly distributed among the water molecules and the result is a homogeneous mixture.

Solutions, then, are homogeneous mixtures of individual molecules or atoms. Since matter exists as a solid, liquid, or gas, many types of solutions are possible. For example, steel is a solution of carbon in iron, or a solid dissolved in a solid; household ammonia is a solution of ammonia gas in water, or a gas dissolved in a liquid. The air we breathe consists mainly of a solution of gases dissolved in a gas. The disinfectant, lysol, is a solution of cresols in water, or a liquid dissolved in a liquid. In a solution, the substance which is dissolved is called the *solute*, while the substance in which the solute is dissolved is called the *solvent*. In a solution of common salt, the salt is the solute and the water is the solvent.

IMPORTANCE OF SOLUTIONS

The most common type of solutions are those in which a liquid is used as the solvent. By far the most important solvent is water; its solutions are called *aqueous solutions*. In the animal body, solutions are of great importance. The contents of living cells, and the food and waste material carried to and from the cells, exist in aqueous solutions. When food is digested in the body, it must be dissolved and carried into the blood stream in solution. The growth of plants depends on the circulation of

Water softeners used in homes, hospitals, laundries, and small industries often employ zeolite or permutit which is a natural sodium aluminum silicate ($\text{Na}_2\text{Al}_2\text{Si}_2\text{O}_3$). The sodium in zeolite is exchanged for the calcium, magnesium, or iron in the hard water as it filters through the softener, thus removing these objectionable impurities. After the zeolite has exchanged all its available sodium for calcium, magnesium, or iron, the original compound may be regenerated for further use by allowing sodium chloride to filter through the zeolite.

REVIEW QUESTIONS

1. List several functions of water in the body.
2. How would you describe dew, fog, frost, and snow from a chemical viewpoint?
3. Of what importance is the fact that ice is lighter than water?
4. Why are the water pipes in an unheated house drained during the winter?
5. For what reason are autoclaves more efficient than boiling water for sterilizing hospital supplies?
6. Why is the scientific thermometer called the centigrade thermometer?
7. Write equations for the reaction between:
 - (a) sodium and water.
 - (b) calcium oxide and water.
 - (c) potassium carbonate and water.
8. Give three examples of hydrates.
9. What happens to a hydrate when it is heated? Illustrate with an example and name the product that is formed.
10. Would a deliquescent or an efflorescent compound make the best drying agent? Explain your reasoning.
11. What property of plaster of paris enables it to be used in the preparation of surgical casts?
12. What method of water purification would you use to prepare: (a) drinking water for a large city; (b) water for the preparation of solutions in the laboratory or hospital?
13. Why does recently boiled water have a flat taste? How can this be remedied?
14. Explain the difference between: (a) hard water and soft water; (b) temporary hard water and permanent hard water.
15. Write equations for the reactions that occur in the softening of (a) permanent hard water; (b) temporary hard water.
16. List several advantages for the use of soft water in the hospital, the home, and in industry.

SUBSTANCE	GRAMS DISSOLVED BY 100 CC. OF WATER AT		
	0° C.	20° C.	100°C.
Potassium nitrate	13.3	31.6	246.0
Copper sulfate	14.3	20.7	75.4
Sodium chloride. . .	35.7	36.0	39.8
Calcium hydroxide	0.185	0.165	0.077

The first two substances show a definite increase in solubility as the temperature is raised, but the solubility of sodium chloride is only slightly affected by the change in temperature. The solubility of calcium hydroxide, on the other hand, decreases with a rise in temperature.

The solubility of gases is decreased by a rise in temperature and is increased by an increase in pressure. In the preparation of carbonated drinks, large amounts of carbon dioxide are forced into solution by pressure at a low temperature. If a cold bottle of soda water is opened, the pressure is released and the gas escapes slowly from the solution, forming bubbles in the water. If a warm bottle is opened, the carbon dioxide escapes rapidly, causing foam to spurt out of the bottle.

TYPES OF SOLUTION

Since solutions are mixtures, their concentration depends entirely upon the amount of solute dissolved in a definite quantity of solvent. When a solution contains a small percentage of the solute that could be dissolved in the solvent, it is said to be *dilute*; when it contains a large percentage, it is said to be *concentrated*. A solution that contains all the solute that can be dissolved at a given temperature is called a *saturated* solution. If a saturated solution is made at a high temperature and is then allowed to cool, the extra solute that was dissolved at the higher temperature usually becomes insoluble and settles out of the solution. If the hot solution is cooled slowly and is not disturbed, the excess solid does not settle out and we have a solution which contains more solute than it can ordinarily dissolve at room temperature. Such a solution is called a *supersaturated* solution. If this solution is disturbed by the addition of a crystal of the solute, the material in excess of that required to saturate the

solutions carrying food and waste material to and from the different parts of the plant. Since practically all chemical reactions take place in solution, it is essential to know their main properties. Many therapeutic agents are administered in the form of solutions to facilitate their absorption into the body, thereby assuring effective reaction.

FACTORS AFFECTING SOLUBILITY

Since we are concerned mainly with solutions that have solid solutes, the factors that influence their solubility will be considered first.

Nature of the Solute and Solvent

It is a well-known fact that our choice of solvent is important when we attempt to dissolve a solid substance. Water is a common solvent for many solutes such as sugar and salts but it is unsatisfactory for fat or paint. Iodine is only slightly soluble in water but will dissolve readily in alcohol. Ether, carbon tetrachloride, and gasoline are good solvents for fatty material, whereas turpentine is used to dissolve paint.

Surface

A finely powdered solute will dissolve more rapidly because more surface is exposed to the solvent.

Agitation

If the mixture is stirred, the rate of solubility of the solute is increased, since fresh solvent is continually coming into contact with the solute.

Temperature

The solubility of most solid solutes increases with a rise in temperature. However, there are some exceptions to this general rule. The following table illustrates the change in solubility of certain solutes at different temperatures:

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solution at that temperature will immediately crystallize out. Freshly prepared jams and jellies are common examples of supersaturated solutions. Upon standing, they may slowly form crystals of sugar.

It is often important to have a more accurate knowledge of the concentration of a solution. A common method of expressing the concentration of a solution is to indicate the grams of solute in 100 cc. of a solution. This is the basis for the *percentage solu-*



Fig. 23. A saturated solution. An excess of solute is present in the beaker, assuring a saturated solution above the solid material. (From Brauer, O. L.: *Chemistry and Its Wonders*. New York, American Book Company.)

tions that are widely used in medical practice. A 10 per cent solution of sodium chloride, for example, would contain 10 gm. of sodium chloride dissolved in water and diluted until the solution had a final volume of 100 cc. Isotonic saline solution is a 0.9 per cent solution of sodium chloride and contains 0.9 gm. of sodium chloride in 100 cc. of solution. To determine the amount of any substance required to prepare a definite volume of a percentage solution, you should start with the number of grams present in 100 cc. For example, to find the amount of glucose

that must be used to prepare 300 cc. of a 5 per cent solution we would proceed as follows:

FIRST STEP: A 5 per cent solution contains 5 gm. in 100 cc.

SECOND STEP: 300 cc. is required.

$$\frac{300}{100} = 3 \text{ times the amount in 100 cc.}$$

$$3 \times 5 \text{ gm.} = 15 \text{ gm.}$$

Therefore 15 gm. is present in 300 cc. of a 5 per cent solution.

A type of solution that is widely used by the chemist is the molar solution. This method of expressing the concentration is convenient because it bears a definite relationship to the molecular weight of the solute. A gram molecular weight of a substance is known as a *mole* of the substance. A solution that contains one mole of the solute in one liter is called a *molar* solution. In calculating the amount of a compound that is used to prepare a given volume of a molar solution, the following scheme may be used:

FIRST STEP: Calculate the molecular weight of the compound and express it in grams

Example: H_2SO_4 $1 + 1 + 32 + 16 + 16 + 16 + 16 = 98$

98 gm. equals 1 gram molecular weight.

SECOND STEP: A 1 molar (1M) solution contains the molecular weight in grams dissolved in 1 liter.

Example: 1M H_2SO_4 contains 98 gm. H_2SO_4 per 1000 cc.

THIRD STEP: To determine the amount of a compound present in a given volume of different molar solution.

Example: 1000 cc. of 0.5M H_2SO_4

$$\frac{0.5\text{M}}{1\text{M}} = \frac{1}{2} \text{ times the amount in 1000 cc. of a 1M solution.}$$

$$\frac{1}{2} \times 98 \text{ gm.} = 49 \text{ gm. } \text{H}_2\text{SO}_4.$$

Therefore 1000 cc. of 0.5M H_2SO_4 contains 49 gm. H_2SO_4 .

Example. 500 cc. of 3M H_2SO_4

$$\frac{3\text{M}}{1\text{M}} = 3 \text{ times the amount in 1000 cc. of a 1M solution.}$$

$$3 \times 98 \text{ gm.} = 294 \text{ gm. } \text{H}_2\text{SO}_4 \text{ in 1000 cc. of 3M } \text{H}_2\text{SO}_4.$$

$$500 \text{ cc. contains } \frac{500 \text{ cc.}}{1000 \text{ cc.}} = \frac{1}{2} \text{ the amount in 1000 cc. of 3M } \text{H}_2\text{SO}_4.$$

$$\frac{1}{2} \times 294 \text{ gm.} = 147 \text{ gm. } \text{H}_2\text{SO}_4.$$

Therefore 500 cc. of 3M H_2SO_4 contains 147 gm. H_2SO_4 .

By the use of molar solutions, we can obtain any desired number of moles of a substance by merely measuring a volume of the solution. Obviously this procedure saves time when several samples of varying concentration are required.

SOME PHYSICAL PROPERTIES OF SOLUTIONS

Diffusion

If we drop a crystal of a colored solute such as potassium permanganate (KMnO_4) in a vessel of water, a purple color is soon observed in the water immediately surrounding the crystal.

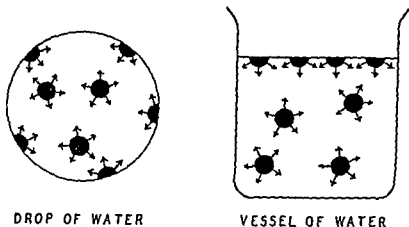


Fig. 24. The surface tension within a single drop of water and within a vessel of water.

In a few hours, the purple color is scattered throughout the entire solution, showing that the molecules of the dissolved solute diffuse or move about freely in the solvent.

Freezing and Boiling Points of a Solution

A solution always has a lower freezing point and a higher boiling point than the pure solvent. Practical use is made of this lowering of the freezing point. For example, the brine or calcium chloride solutions used in refrigeration freeze at a much lower temperature than water. In the manufacture of ice, the circulation of brine can lower the freezing temperature to -21°C . and is often

employed in making ice cream. The so-called antifreeze compounds that are used in automobile radiators are merely substances like alcohol and glycerol that lower the freezing point of the circulating water and prevent its freezing in the winter.

Surface Tension

The molecules of a solution are constantly attracted to each other. A molecule in the center of a solution is completely surrounded by other molecules and is therefore equally attracted from all sides. A molecule near the surface of the solution (Fig. 24) is attracted downward more strongly because there are more molecules in the solution below it than in the air above the surface. This downward pull on the surface molecules causes them to pack tightly together to form a surface film. *Surface tension* is the force or tension required to break this film. Water has a higher surface tension than most liquids, in fact the parlor trick of floating a steel needle on water is made possible by the strength of its surface film.

Osmosis

Many plant or animal membranes are semipermeable in that they allow one component of a solution to pass through, while

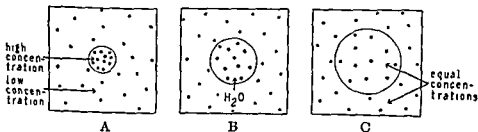


Fig. 25. Osmosis. A, the solution within the membrane has a higher concentration of salts than the solution on the outside. B, in the process of osmosis, water flows into the solution of high concentration until the concentrations are equalized, C.

they hold back another component. The roots of a plant are covered with a semipermeable membrane that allows the passage of water into the plant but will not allow the substances in the

sap to pass out into the ground. If the solutions on either side of a semipermeable membrane are unequal in concentration, there is a tendency to equalize the concentration. The diffusible component, usually water, will tend to flow from the more dilute solution into the concentrated solution. This selective flow of a diffusible component through a membrane is called *osmosis*; the pressure exerted by the movement of the component is called the *osmotic pressure*. The osmotic pressure of a solution is proportional to the amount of solute dissolved in the solution. When the solutions on each side of a semipermeable membrane have established equilibrium and have an equal concentration of components, they are said to be *isotonic*.

ISOTONIC SALT SOLUTION

The normal concentration of salts in the blood is approximately equivalent to a 0.9 per cent sodium chloride solution.

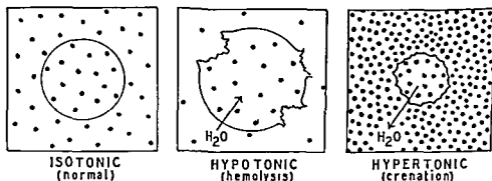


Fig. 26. A simple representation of the changes that occur in the red blood cell when it is suspended in an isotonic, a hypotonic, and a hypertonic solution.

Very little osmosis occurs when living tissues are in contact with a salt solution of this strength. A 0.9 per cent solution of sodium chloride is therefore called an *isotonic salt solution*. When blood is mixed with an isotonic salt solution, there is an equilibrium between the 0.9 per cent salt solution on one side of the red cell membrane and the cell contents on the other side. Therefore, no osmosis occurs, the red corpuscles do not change in size or

shape, and the isotonic salt solution is isotonic with respect to the red blood cell.

If a solution contains a lower concentration of salt than the blood, it is said to be *hypotonic*. Distilled water is an example of a hypotonic solution. When blood is mixed with a hypotonic solution, the corpuscles begin to swell and finally rupture. Since the two solutions on either side of the cell membrane are of unequal concentration, osmosis occurs and water flows into the cell from the lower to the higher concentration. This causes dilution of the cell contents and the cell increases in size until it bursts. This disintegration of corpuscles in a hypotonic solution is called *hemolysis* and the blood is said to be *laked*.

A solution that contains a higher percentage of salt than the blood is called a *hypertonic* solution. A 5 per cent solution of sodium chloride would be an example of a hypertonic solution. When blood is mixed with a hypertonic solution, the water in the cell contents flows out through the cell membrane into the solution of higher concentration. This causes the cell to decrease in size; this shrinking of corpuscles in a hypertonic solution is called *crenation*.

It is evident from the previous discussion that solutions cannot be safely introduced into the blood stream unless they are practically isotonic with respect to the corpuscles. When drugs are administered intravenously, they are often dissolved in isotonic salt solution. A sterile isotonic salt solution is commonly used to cleanse wounds to prevent changes in the tissues by osmosis. After hemorrhage, the fluid content of the circulatory system is often increased by the injection of sterile isotonic salt solution.

TRUE SOLUTIONS, COLLOIDAL SOLUTIONS, AND SUSPENSIONS

In a *true solution*, the solute dissolves in the solvent to form a homogeneous mixture of individual molecules. As has already been stated, the particles of the dissolved substance are too small to be seen and will never settle out of the solution. When a solid solute does not dissolve in the solvent and the particles are so

large that they can be seen with the naked eye, the mixture is called a *suspension*. The solid substance usually settles to the bottom of the solvent on standing. Many finely divided solute



Fig. 27. The electron microscope, 50 to 100 times more powerful than the best light microscope, includes a diffraction camera. Seated are Dr. V. K. Zworykin (left) and Dr. James Hillier and standing is P. C. Smith, the men largely responsible for the development of the electron microscope in this country. (Courtesy of R.C.A., Camden, N. J.)

which do not dissolve in the solvent have particles so small that they will not settle out of the mixture on standing and cannot be seen with the naked eye. These substances whose particles

are intermediate in size between those in true solutions and in suspensions, are called *colloids*; when mixed with a solvent they form *colloidal solutions*. Such solutions are more accurately called colloidal dispersions since the solute does not dissolve in the solvent.

The particles in the three types of solutions would, therefore, vary from molecular size in the true solution to a large visible



Fig 28 Upper, *Streptococcus hemolyticus* magnified 25,000 diameters. Lower, *Mycobacterium tuberculosis* (human) magnified 42,000 times. The limit of magnification of the ordinary microscope is 2000 diameters compared to a possible magnification of 200,000 diameters with the electron microscope. (Courtesy of E. R. Squibb & Sons)

particle in the suspensions. Colloidal particles are so small that they cannot be seen with an ordinary microscope; however, the particles of some colloids have been made visible by the use of the electron microscope (Figs. 27 and 28). In a true solution, the particles will pass through membranes and filters; in a colloidal solution, the particles will pass through a filter but not through a membrane; and in suspensions, the particles will not pass through filters or membranes.

PROPERTIES OF COLLOIDS

Size

The term colloid indicates a state of matter. Any substance that is subdivided into particles ranging in size from 1 to 100 millimicrons is a colloid. (A millimicron is one-millionth of a millimeter.) Particles of this size have a relatively large surface compared with their small weight. For example, if we subdivided a tennis ball into pieces the size of colloidal particles and spread them in a layer, they would cover a surface equal to 20 tennis courts. Powdered charcoal is an example of a colloid whose particles have an extremely large surface in comparison to their weight.

Adsorption

A characteristic property of colloids is their ability to adsorb or take up other substances on their surfaces. This process is called *adsorption* and has many practical applications. For instance, charcoal is used in gas masks to adsorb poisonous gases, and in tablets to aid in the treatment of indigestion. Some cities use charcoal to remove gases and offensive odors from their water supply. A medical preparation such as argyrol contains colloidal silver adsorbed on a protein.

Dialysis

Substances that dissolve to form true solutions are often called *crystalloids* to distinguish them from colloids. Crystalloids will readily pass through membranes that hold back the colloidal particles. In general, such membranes can be considered as sieves with holes of a definite size. If the substance to be diffused through the membrane has particles smaller than the holes, as in the case of a crystalloid, it will readily pass through, but colloidal particles larger than the holes are withheld. If a solution containing both crystalloids and colloids is placed in a parchment bag and the bag is suspended in a beaker of distilled water, the crystalloids will pass through the membrane into the distilled water while the colloids will remain in the bag. The membrane is called a *dialyzing membrane* and the process of separation of the

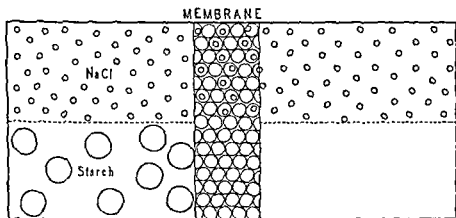


Fig. 29. The process of dialysis. The crystalloid particles, NaCl , readily pass through the holes in the membrane, while the colloidal particles of starch are held back.

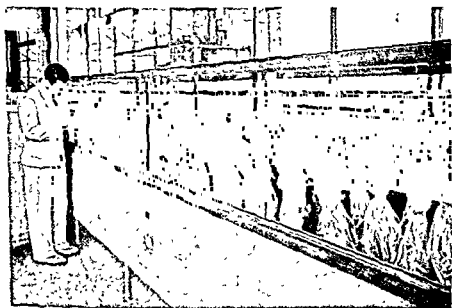


Fig. 30. Large scale dialysis in the manufacture of antitoxin. (Courtesy of Parke Davis & Company, Detroit.)

crystalloids from the colloids is called *dialysis*. This process is represented in Fig. 29, in which sodium chloride is used as an example of a crystalloid and starch as a colloid.

Most animal membranes may be regarded as dialyzing membranes. In the human body, the process of absorption of the digested food material takes place through the mucous membrane of the intestinal wall. As long as the food remains in a colloidal solution, it cannot dialyze through the membrane. The process of digestion converts the food into crystalloidal material that can pass through the intestinal wall into the blood stream. Many other processes in the body such as respiration, distribution of food and waste material by the blood, formation of urine by the kidneys, and the proper distribution of fluid in the tissues depend upon the passage of substances through membranes.

Gels

Certain colloidal solutions as gelatin and agar are liquid when freshly made but solidify on standing to form a jelly-like material. This semisolid substance retains the water that was used to prepare the solution and is called a *gel*. Common examples of gels in the home are fruit jellies, gelatin desserts, custards, and cornstarch puddings.

Emulsions

If we shake together two liquids that do not mix, as oil and water, the result is a milky appearing solution called an *emulsion*. Small globules of oil remain suspended in the water for a short time but the two liquids soon separate. For this reason, a mixture of oil and water is called a *temporary emulsion*. Milk and cream are examples of *permanent emulsions*. If a certain type of colloid is added to a temporary emulsion, it coats the globules of the fat or oil and prevents them from running together, thus making a more permanent emulsion. A small amount of a soap solution will make a permanent emulsion of oil and water. Colloids that act in this fashion are called *emulsifying agents*. Milk is an emulsion of butter fat in water with casein acting as an emulsifying agent. Mayonnaise is an emulsion of oils and vinegar to which the colloids of egg yolks are added as emulsifying agents.

IMPORTANCE OF COLLOIDS

A knowledge of colloids is important from both a chemical and physiological standpoint. Colloidal chemistry is essential for an understanding of oils, greases, soaps, starch, paints, lacquers, rubber, textiles, leather, cream, milk, and many pharmaceutical products used as medications. Such processes as cooking, washing, dyeing of fabrics, water purification, and sewage disposal are more readily explained by the use of colloidal chemistry.

It is difficult to estimate the extent of the influence of colloids on physiological processes. The tissues of the body are colloidal in nature; therefore many of the reactions that occur in the tissues involve colloidal chemistry. For example, the digestion of food begins as a colloidal process, the food first forming a colloidal solution before it is completely digested into small molecules. The contraction of muscle tissue during movement of the body is governed by a colloidal phenomena. Abnormal conditions such as edema, pain, headaches, and certain diseases are closely related to colloidal chemistry.

Colloidal chemistry, therefore, is an important division of chemistry and a more thorough understanding of its principles will aid in the intelligent treatment of the ills of the human body.

REVIEW QUESTIONS

1. Name four types of solutions. For each type give an example not mentioned in the book.
2. Define solution, solute, and solvent.
3. Given a dry solid that is soluble in water, what factors influence the solubility of the solid? How would you proceed to prepare a solution of the substance in the shortest possible time?
4. Why are bottles of carbonated beverages cooled before removing the caps?
5. Distinguish between the following terms. (a) dilute and concentrated, (b) saturated and supersaturated.
6. How many grams of cane sugar would be required to prepare 500 cc of a 10 per cent solution?
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8. One liter (1000 cc.) of 2M sodium hydroxide contains how many grams of sodium hydroxide?

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9. How many grams of sulfuric acid (H_2SO_4) are there in 400 cc. of a 0.5M solution?
10. Explain your conception of surface tension, osmosis, and osmotic pressure.
11. Why is physiological salt solution said to be isotonic with respect to the red blood cell?
12. What changes would occur in the blood if a hypertonic solution were injected intravenously? A hypotonic solution?
13. Outline the main differences between true solutions, colloids, and suspensions.
14. Of what physiological importance is the process of dialysis? Can you suggest a practical application of dialysis in the field of medicine?
15. List several examples of emulsions that are encountered in the home and in the hospital. What type of pharmaceutical products are usually permanent emulsions?

CHAPTER VIII

Acids, Bases, and Salts

THERE are over 25,000 inorganic compounds known to the chemist. It would be practically impossible for anyone to learn the composition and properties of each compound. The study of inorganic chemistry has been greatly simplified by the fact that almost all of these compounds can be divided into three groups. These fundamental groups of compounds are known as acids, bases, and salts.

ACIDS

We ordinarily think of acids as existing in the liquid state, but they may exist in any of the three states of matter (solid, liquid, or gaseous). Boric acid, for example, is a solid; sulfuric acid is a liquid, and hydrochloric acid is a solution of the gas, hydrogen chloride. As a rule, acids are not very reactive unless they are in solution. The following list will help us to understand the composition of some of the common acids:

ACID	FORMULA
Hydrochloric acid	HCl
Hydrobromic acid	HBr
Nitric acid	HNO ₃
Carbonic acid	H ₂ CO ₃
Sulfuric acid	H ₂ SO ₄
Phosphoric acid	H ₃ PO ₄
Boric acid	H ₃ BO ₃

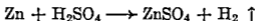
From the above formulas, it can be seen that acids consist of hydrogen combined with another element or with a radical. The element or radical that is combined with hydrogen in an acid is called the *acid radical*.

Properties of Acids

1. All acids in solution have a sour taste. Citrus fruits, for example, taste sour because of the presence of the organic acid, citric acid. The sour taste of vinegar is due to acetic acid.

2. Acids change the blue color of litmus dye to red. This is one of the simplest tests for the presence of an acid. A substance like litmus that has one color in an acid solution and another color in a basic solution is called an *indicator*.

3. Acids react with many metals to form hydrogen gas. The metal replaces the hydrogen of the acid, liberating hydrogen gas. For example, in the following reaction zinc replaces the hydrogen of sulfuric acid to form zinc sulfate and gaseous hydrogen:



Not all of the metals possess enough chemical activity to replace the hydrogen of an acid. The following table lists some of the common metals in the order of their activity. Those metals above hydrogen will replace it from an acid; those below hydrogen will not:

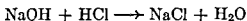
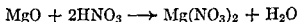
Potassium	High activity
Sodium	
Calcium	
Magnesium	
Aluminum	
Zinc	
Iron	
Lead	
Hydrogen	
Copper	
Mercury	
Silver	
Platinum	
Gold	Low activity

This series is commonly known as the *electromotive series*. Since the hydrogen of an acid may be replaced by most metals we can enlarge our definition of an acid to include the fact that the hydrogen of an acid is *replaceable hydrogen*.

Acids react with all of the common industrial metals and should not be allowed to come in contact with surgical instru-

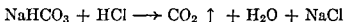
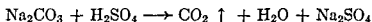
ments or metal containers. All laboratory reactions that involve acids are carried out in glass vessels.

4 Acids react with oxides and hydroxides to form water and a salt. The action of an acid on an oxide or hydroxide of a metal may be represented as follows:



In the reaction between an acid and a metallic hydroxide, or base, both the acid and the base are neutralized. A reaction of an acid and a base to form water and a salt is therefore called a *neutralization reaction*.

5. Acids react with carbonates and bicarbonates to form carbon dioxide gas. Sodium carbonate (Na_2CO_3) or washing soda, and sodium bicarbonate (NaHCO_3) or baking soda, react with acids to form carbon dioxide gas, water, and a salt.



Baking soda is widely used for the neutralization of acid and for the production of carbon dioxide gas. A great many patent medicines for the relief of pain, indigestion, and constipation contain bicarbonates that neutralize the acid in the stomach. Neutralization of the acid in the stomach by frequent use of sodium bicarbonate interferes with gastric digestion and may result in more serious disturbances. Baking powders contain a bicarbonate and some acid-forming substance, which, when moisture is added, release gaseous carbon dioxide throughout the cake batter, making it light. The lactic acid of sour milk produces the same effect when mixed with baking soda. The action of a common type of fire extinguisher depends upon the reaction between sulfuric acid and sodium bicarbonate.

The Naming of Acids

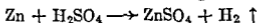
Acids composed of hydrogen and one other element are called *binary* or *hydro-acids*. They are named from the second element

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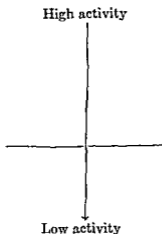
2. Acids change the blue color of litmus dye to red. This is one of the simplest tests for the presence of an acid. A substance like litmus that has one color in an acid solution and another color in a basic solution is called an *indicator*.

3. Acids react with many metals to form hydrogen gas. The metal replaces the hydrogen of the acid, liberating hydrogen gas. For example, in the following reaction zinc replaces the hydrogen of sulfuric acid to form zinc sulfate and gaseous hydrogen:



Not all of the metals possess enough chemical activity to replace the hydrogen of an acid. The following table lists some of the common metals in the order of their activity. Those metals above hydrogen will replace it from an acid; those below hydrogen will not:

Potassium
Sodium
Calcium
Magnesium
Aluminum
Zinc
Iron
Lead
Hydrogen
Copper
Mercury
Silver
Platinum
Gold

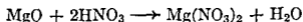


This series is commonly known as the *electromotive series*. Since the hydrogen of an acid may be replaced by most metals we can enlarge our definition of an acid to include the fact that the hydrogen of an acid is *replaceable hydrogen*.

Acids react with all of the common industrial metals and should not be allowed to come in contact with surgical instru-

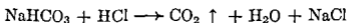
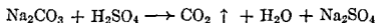
ments or metal containers. All laboratory reactions that involve acids are carried out in glass vessels.

4. Acids react with oxides and hydroxides to form water and a salt. The action of an acid on an oxide or hydroxide of a metal may be represented as follows:



In the reaction between an acid and a metallic hydroxide, or base, both the acid and the base are neutralized. A reaction of an acid and a base to form water and a salt is therefore called a *neutralization reaction*.

5. Acids react with carbonates and bicarbonates to form carbon dioxide gas. Sodium carbonate (Na_2CO_3) or washing soda, and sodium bicarbonate (NaHCO_3) or baking soda, react with acids to form carbon dioxide gas, water, and a salt.



Baking soda is widely used for the neutralization of acid and for the production of carbon dioxide gas. A great many patent medicines for the relief of pain, indigestion, and constipation contain bicarbonates that neutralize the acid in the stomach. Neutralization of the acid in the stomach by frequent use of sodium bicarbonate interferes with gastric digestion and may result in more serious disturbances. Baking powders contain a bicarbonate and some acid-forming substance, which, when moisture is added, release gaseous carbon dioxide throughout the cake batter, making it light. The lactic acid of sour milk produces the same effect when mixed with baking soda. The action of a common type of fire extinguisher depends upon the reaction between sulfuric acid and sodium bicarbonate.

The Naming of Acids

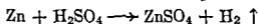
Acids composed of hydrogen and one other element are called *binary* or *hydro-acids*. They are named from the second element

Properties of Acids

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2. Acids change the blue color of litmus dye to red. This is one of the simplest tests for the presence of an acid. A substance like litmus that has one color in an acid solution and another color in a basic solution is called an *indicator*.

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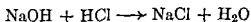
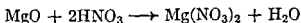
Potassium	High activity
Sodium	
Calcium	
Magnesium	
Aluminum	
Zinc	
Iron	
Lead	
Hydrogen	
Copper	
Mercury	
Silver	
Platinum	
Gold	Low activity

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Acids react with all of the common industrial metals and should not be allowed to come in contact with surgical instru-

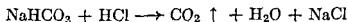
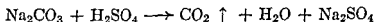
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The Naming of Acids

Acids composed of hydrogen and one other element are called *binary* or *hydro-acids*. They are named from the second element

and always begin with the prefix hydro- and end with the suffix -ic. Examples:

H Cl
Hydro-chlor-ic

H Br
Hydro-brom-ic

H F
Hydro-fluor-ic

Many acids contain oxygen in addition to hydrogen and another element and are called *ternary* or *oxy-acids*. Such acids are named after the element other than hydrogen or oxygen and end with the suffix -ic. Examples:

H_2SO_4
Sulfur-ic

H_3PO_4
Phosphor-ic

H_2CO_3
Carbon-ic

If the same three elements unite to form more than one ternary acid, the acid with the greatest number of oxygen atoms ends in -ic, while the acid with the lowest number of oxygen atoms ends in -ous. Examples:

HNO_3
Nitr-ic

H_2SO_4
Sulfur-ic

HNO_2
Nitr-ous

H_2SO_3
Sulfur-ous

BASES

Bases are compounds which contain the hydroxyl radical combined with a metal or with the ammonium radical. They are often referred to as alkalis; a solution containing a base is called a basic or alkaline solution. The following table contains a few of the common bases:

BASE	FORMULA
Sodium hydroxide.	NaOH
Potassium hydroxide.	KOH
Magnesium hydroxide.	$\text{Mg}(\text{OH})_2$
Calcium hydroxide	$\text{Ca}(\text{OH})_2$
Ammonium hydroxide.	NH_4OH

With the exception of ammonium hydroxide, all bases are hydroxides of metals and exist as solids.

Properties of Bases

1. When a base is dissolved in water, the solution has a slippery feeling.
2. Solutions of bases have a bitter, metallic taste.
3. Bases change the red color of litmus to a blue. In general, bases reverse the color change that was produced by an acid in an indicator.
4. Bases react with acids to form water and a salt:



This is another example of a neutralization reaction.

The Naming of Bases

Since bases consist of a metal combined with the hydroxyl radical, they are named by starting with the name of the metal and ending with the word *hydroxide*. For example, NaOH is sodium hydroxide, KOH is potassium hydroxide, and $\text{Ca}(\text{OH})_2$ is calcium hydroxide. (The only exception to this rule concerns the base that does not contain a metal; this is named ammonium hydroxide in a similar fashion.)

ACTION OF ACIDS AND BASES ON TISSUES

Strong acids (sulfuric, nitric, and hydrochloric) and strong bases (sodium and potassium hydroxide) will destroy tissues by dissolving their protein material and extracting their water. Basic solutions will also combine with any fats that are present. Household lye (crude NaOH) is a common example of a strong base. This substance is very caustic and must be handled carefully to prevent damage to the skin.

If strong acids or bases are spilled on the skin, a serious burn may result. In either case, the area should be flooded with water to remove quickly any of the acid or base that has not combined with the tissue. In the case of acid burns, a weak alkaline solution should then be applied to neutralize any acid that remains on the skin. Dilute ammonia water (NH_4OH), limewater [$\text{Ca}(\text{OH})_2$] or baking soda (NaHCO_3) are effective weak bases that

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H Cl
Hydro-chlor-ic

H Br
Hydro-brom-ic

H F
Hydro-fluor-ic

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Phosphor-ic

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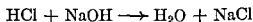
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may be applied without injury to the skin. In the treatment of alkali burns, the excess alkali remaining on the skin should be neutralized with a dilute acid. The acetic acid in vinegar or a boric acid solution may be safely used. A very dilute solution of a strong acid may be used, but care should be taken to prevent further injury to the tissues from a solution that is too concentrated.

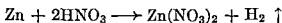
Animal fibers, such as wool, or silk, are also proteins and are attacked by acids or bases. Silk or woolen materials cannot be washed in strong laundry soaps because the soap contains some free base; this may cause them to shrink and may also partially dissolve the fabrics. Basic substances such as lye, washing soda, and ammonia are often used as cleaning agents because of their ability to dissolve protein and fats.

SALTS

When an acid and a base react with each other they form water and a salt.



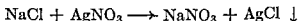
Salts may also be formed by the displacement of hydrogen from an acid with a metal.



We may define *salts* as compounds formed by replacing the hydrogen of an acid with a metal.

Reactions of Salts

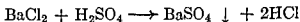
1. Salts react with each other to form new salts.



This is a common reaction in chemistry and is used as a test for the presence of a chloride. When silver nitrate is added to a solution that contains chlorides, a positive test is indicated by the formation of a white precipitate (insoluble AgCl). Silver nitrate solutions are used therapeutically as germicides. One drop of a 1 per cent solution of silver nitrate is placed in the eyes

of newborn babies to prevent gonorrheal infections. It is also often used in bladder infections, but its germicidal activity is stopped when it reacts with the sodium chloride in the urine to form the insoluble silver chloride.

2. Salts react with acids to form other salts and other acids.



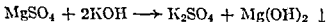
The insoluble barium sulfate formed in this reaction is opaque to x-rays. When given patients by mouth, it coats the stomach and



Fig. 31. Carcinoma of the colon diagnosed from an x-ray photograph of the large intestine filled with barium sulfate solution. (From Farrell, J. T., Jr.: Roentgen Diagnosis of Diseases of the Gastrointestinal Tract, Springfield, Ill., Charles C Thomas, Publisher.)

intestine, outlining them on the x-ray photograph. It is commonly used as a diagnostic aid in the detection of ulcers and cancer in the gastro-intestinal tract (Fig. 31).

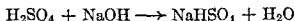
3. Salts react with bases to form other salts and other bases.



Magnesium hydroxide, the insoluble base formed in this reaction, is often used in medicine. When mixed with water, it forms a suspension, known as milk of magnesia. Since it is a weak base, milk of magnesia is often used to neutralize excess acid in the stomach.

Normal and Acid Salts

A *normal* salt is one in which all the hydrogen of an acid has been replaced by a metal. For instance, all the salts in the three reactions just discussed are normal salts. Salts formed from acids that contain more than one replaceable hydrogen atom may retain one or more hydrogen atoms in their molecule and are called *acid salts*. For example, sulfuric acid may react with sodium hydroxide to form sodium acid sulfate, which is commonly called sodium bisulfate or sodium hydrogen sulfate.



If both hydrogen atoms are replaced by sodium, the normal salt sodium sulfate is formed.



Other examples of acid salts are sodium bicarbonate (NaHCO_3), sodium dihydrogen phosphate (NaH_2PO_4), and disodium hydrogen phosphate (Na_2HPO_4). The latter two compounds are made from phosphoric acid, which has three replaceable hydrogen atoms; therefore two acid salts are possible.

The Naming of Salts

Normal salts that are formed from binary acids are named by starting with the name of the metal or ammonium radical and ending the name of the nonmetal with the suffix *-ide*. For example, sodium chloride for NaCl , ammonium chloride for NH_4Cl , potassium bromide for KBr , and potassium iodide for KI . If the metal has more than one valence, the endings *-ous* and *-ic* are used after the name of the metal. A salt in which the metal has the lower valence contains the suffix *-ous*, while the salt of the metal with the higher valence uses the suffix *-ic*.

Mercury has a valence of +1 or +2 and its salts are named mercurous chloride for HgCl and mercuric chloride for HgCl_2 . In a similar fashion, iron salts in which the iron has a valence of +2 or +3 are named ferrous chloride for FeCl_2 and ferric chloride for FeCl_3 .

The names of salts derived from ternary acids depend on the name of the acid. If the name of the acid ends in *-ic*, the name of the salt ends in *-ate*:

HNO_3 , nitric acid . . .	NaNO_3 , sodium nitrate
H_2CO_3 , carbonic acid . . .	K_2CO_3 , potassium carbonate
H_2SO_4 , sulfuric acid	BaSO_4 , barium sulfate

If the name of the acid ends in *-ous*, the name of the salt ends in *-ite*:

HNO_2 , nitrous acid . . .	NaNO_2 , sodium nitrite
H_2SO_3 , sulfurous acid	BaSO_3 , barium sulfite

This type of salt may also be named from the acid radical in the acid from which the salt was formed. The following radicals would form salts named as follows.

SO_4 , sulfate radical	Na_2SO_4 , sodium sulfate
CO_3 , carbonate radical . . .	CaCO_3 , calcium carbonate
NO_2 , nitrite radical . . .	KNO_2 , potassium nitrite
PO_4 , phosphate radical	AlPO_4 , aluminum phosphate
SO_3 , sulfite radical . .	K_2SO_3 , potassium sulfite
NO_3 , nitrate radical	$\text{Ba}(\text{NO}_3)_2$, barium nitrate

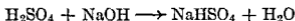
When the metal has more than one valence, these salts are named in a similar fashion to those derived from binary acids. For example, HgNO_3 would be named mercurous nitrate, $\text{Hg}(\text{NO}_3)_2$ would be named mercuric nitrate, and Hg_2SO_3 would be named mercurous sulfite.

Acid salts are named like normal salts except that the name of the radical is preceded by the prefix *bi-*, the word *hydrogen*, or the word *acid*. The acid salt NaHSO_4 is named sodium bisulfate, sodium hydrogen sulfate, or sodium acid sulfate. The common prefix is *bi-* as in sodium bicarbonate NaHCO_3 , and potassium bisulfite KHSO_3 .

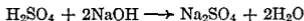
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Normal and Acid Salts

A *normal* salt is one in which all the hydrogen of an acid has been replaced by a metal. For instance, all the salts in the three reactions just discussed are normal salts. Salts formed from acids that contain more than one replaceable hydrogen atom may retain one or more hydrogen atoms in their molecule and are called *acid salts*. For example, sulfuric acid may react with sodium hydroxide to form sodium acid sulfate, which is commonly called sodium bisulfate or sodium hydrogen sulfate.



If both hydrogen atoms are replaced by sodium, the normal salt sodium sulfate is formed.

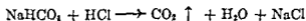


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molecular weight of hydrochloric acid as shown in the following equation, how many grams of hydrochloric acid would be neutralized by 10 gm. of sodium bicarbonate?



7. List the four outstanding characteristics of a base
8. How would you proceed with an emergency treatment of a burn caused by household lye?
9. Why is laundry soap not used to wash the face?
10. What is the difference between an acid salt and a normal salt?
11. Give several examples in which a salt is used in the home and in the hospital
12. Write the equations for the reaction of potassium hydroxide with phosphoric acid to form three different salts.
13. Name the following acids and bases:

HCl	NaOH	Al(OH) ₃
HNO ₃	H ₂ SO ₄	HNO ₂
H ₂ SO ₃	H ₂ CO ₃	H ₃ PO ₄

14. Name the following salts:

HgNO ₂	Fe(NO ₂) ₃	KHSO ₃
AgCl	HgSO ₄	CuCl
CuSO ₄	AlPO ₄	Na ₂ HPO ₄
Na ₂ SO ₃	K ₂ CO ₃	Al ₂ (SO ₄) ₃
MgBr ₂	Ca(HCO ₃) ₂	Ba(HSO ₄) ₂

15. Write the formulas for the following compounds:

Hydrobromic acid	Ferric sulfate
Ammonium carbonate	Potassium bicarbonate
Cuprous sulfite	Calcium hydroxide
Sodium dihydrogen phosphate	Aluminum nitrite
Mercuric nitrate	Barium phosphate

Importance of Salts

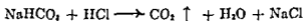
Many salts have important uses in the practice of medicine. The following table lists some common salts and their use in medicine.

Salt	Formula	Common Name	Uses
Ammonium chloride	NH_4Cl		Expectorant
Barium sulfate	BaSO_4	"Barium"	Coats the intestinal tract with a compound opaque to x-rays
Calcium carbonate	CaCO_3	Precipitated Chalk	Antacid, in gastric ulcers
Calcium sulfate	$(\text{CaSO}_4)_2\text{H}_2\text{O}$	Plaster of Paris	Casts and molds
Magnesium carbonate	MgCO_3		Antacid, cosmetic
Magnesium sulfate	MgSO_4	Epsom salts	Cathartic
Mercuric chloride	HgCl_2	Bichloride of mercury	Disinfectant
Mercurous chloride	Hg_2Cl_2	Calomel	Cathartic
Potassium iodide	KI		Expectorant
Potassium nitrate	KNO_3	Saltpeter	Diuretic
Silver nitrate	AgNO_3	Lunar caustic	Antiseptic: astringent
Sodium bicarbonate	NaHCO_3	Baking soda	Antacid in hyperacidity
Sodium chloride	NaCl	Table salt	Saline solution

REVIEW QUESTIONS

1. Into what three fundamental groups are most inorganic compounds divided?
2. Define the terms: acid radical, indicator, and replaceable hydrogen.
3. List the outstanding characteristics of an acid.
4. Why should surgical instruments not be allowed to stand in acid solutions or in a solution of copper sulfate? Write the equations for the reaction between iron and hydrochloric acid, and iron and copper sulfate.
5. Write the equation for a typical neutralization reaction.
6. If 1 gram molecular weight of sodium bicarbonate will neutralize 1 gram

molecular weight of hydrochloric acid as shown in the following equation, how many grams of hydrochloric acid would be neutralized by 10 gm. of sodium bicarbonate?



7. List the four outstanding characteristics of a base.
8. How would you proceed with an emergency treatment of a burn caused by household lye?
9. Why is laundry soap not used to wash the face?
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AgCl	HgSO ₄	CuCl
CuSO ₄	AlPO ₄	Na ₂ HPO ₄
Na ₂ SO ₃	K ₂ CO ₃	Al ₂ (SO ₄) ₃
MgBr ₂	Ca(HCO ₃) ₂	Ba(HSO ₄) ₂

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Magnesium carbonate	MgCO_3		Antacid, cosmetic
Magnesium sulfate	MgSO_4	Epsom salts	Cathartic
Mercuric chloride	HgCl_2	Bichloride of mercury	Disinfectant
Mercurous chloride	Hg_2Cl_2	Calomel	Cathartic
Potassium iodide	KI		Expectorant
Potassium nitrate	KNO_3	Saltpeter	Diuretic
Silver nitrate	AgNO_3	Lunar caustic	Antiseptic; astringent
Sodium bicarbonate	NaHCO_3	Baking soda	Antacid in hyper-acidity
Sodium chloride	NaCl	Table salt	Saline solution

REVIEW QUESTIONS

1. Into what three fundamental groups are most inorganic compounds divided?
2. Define the terms: acid radical, indicator, and replaceable hydrogen.
3. List the outstanding characteristics of an acid.
4. Why should surgical instruments not be allowed to stand in acid solutions or in a solution of copper sulfate? Write the equations for the reaction between iron and hydrochloric acid, and iron and copper sulfate.
5. Write the equation for a typical neutralization reaction.
6. If 1 gram molecular weight of sodium bicarbonate will neutralize 1 gram

in distilled water or solutions of sugar, alcohol, or glycerol. Substances whose solutions will conduct an electric current are called *electrolytes*. A compound whose solution will not conduct the

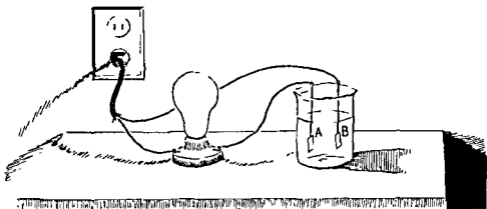


Fig. 32. A simple conductivity apparatus.

current is called a *nonelectrolyte*. In general, compounds other than acids, bases, and salts are classified as nonelectrolytes.

THEORY OF IONIZATION

In 1887, Arrhenius, a Swedish chemist, proposed a theory to explain how an electrolyte in solution conducts an electric current. He reasoned that when an electrolyte dissolved in water, its molecule is split or dissociated into positively charged particles and negatively charged particles. These particles were assumed to be the atoms and radicals that made up the original molecule; the electrical charge they carried was numerically equal to their valence. The electrically charged atoms and radicals were called *ions* and had different properties than the corresponding uncharged particles. He stated also that the total number of positively charged particles always equals the total number of negatively charged particles. The formation of ions in a solution was called *ionization* and may be represented as follows:

CHAPTER IX

Electrolytes and Ionization

IN THE discussion of atomic structure, it was stated that the atom consisted of a nucleus, containing positively charged protons, around which revolved negatively charged electrons. The proton and the electron are the fundamental charges of electricity. They are electrically equivalent although they differ greatly in mass, the proton weighing approximately 1845 times as much as the electron. It is more convenient to speak of a positive charge of electricity than the charge of the proton. Also, a negative charge of electricity is a more common term than the charge of the electron.

Substances that readily allow electricity to pass through them are called *conductors*. Metals such as copper, silver, gold, and iron are good conductors of electricity. Other substances prevent the flow of electricity and are called *insulators*. Non-metallic elements and materials such as glass, porcelain, rubber, and silk are examples of insulators.

ELECTROLYTES

A simple apparatus for demonstrating the conductivity of a solution is shown in Fig. 32. It consists of a source of current connected to a light bulb in such a way that the bulb will not burn until a conductor is placed between the electrodes A and B. If the solution being tested will conduct the electric current, the open circuit between the two electrodes is completed and the light bulb will glow. Solutions of acids, bases, and salts are found to conduct an electric current readily and cause the bulb to burn brilliantly. The bulb will not light when the electrodes are placed

in distilled water or solutions of sugar, alcohol, or glycerol. Substances whose solutions will conduct an electric current are called *electrolytes*. A compound whose solution will not conduct the

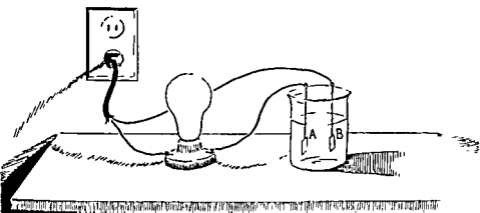
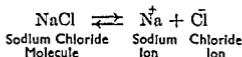


Fig. 32. A simple conductivity apparatus

current is called a *nonelectrolyte*. In general, compounds other than acids, bases, and salts are classified as nonelectrolytes.

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The sodium chloride molecule dissolves in water and dissociates or ionizes to form sodium ions and chloride ions. The valence of sodium is $+1$, of chloride is -1 ; therefore the charge on the sodium ion is $+1$ and on the chloride ion -1 . These ions are free to move about in the liquid independent of each other and may recombine to form salt molecules. Since ionization is rarely complete, a solution of an electrolyte always contains both molecules and ions. An ionization equation is therefore written with a double arrow to indicate the presence of molecules and ions

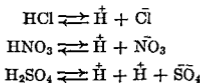
To summarize: When an electrolyte is dissolved in water it dissociates into a large number of electrically charged ions which distribute themselves throughout the solution. The ions readily conduct an electric current across two electrodes as previously described. Solutions of nonelectrolytes do not contain ions and therefore cannot conduct a current.

It should be stressed that the properties of an ion are different from the properties of an uncharged atom. The hydrogen ion (H^+) has a sour taste, while the hydrogen atom has no taste. The cupric ion (Cu^{++}) is blue, while the copper atom is copper colored. The silver ion (Ag^+) is soluble in water, however silver metal is not. When an atom takes on an electric charge and exists as an ion it always assumes new properties.

THE IONIZATION OF ELECTROLYTES

Acids

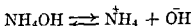
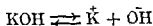
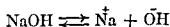
The ionization of some common acids may be represented as follows:



From these equations, we can see that the hydrogen ion is always formed when acids ionize. The hydrogen ion then is common to all acids and must be responsible for the acid properties. Therefore we can further define acids as compounds that form hydrogen ions in water solutions.

Bases

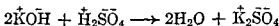
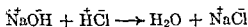
The common bases dissociate into ions when in solution as follows:



The hydroxyl ion is shown to be common to all bases; therefore the properties of a basic solution are due to this ion. Bases may be defined as compounds whose solutions form hydroxyl ions.

Neutralization

A neutralization reaction between an acid and a base can be represented by an ionic equation.

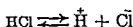


The hydrogen ions of the acids unite with the hydroxyl ions of the base to form water molecules, which are not ionized. The neutralized solution has neither acidic nor basic properties, since hydrogen ions and hydroxyl ions are no longer present but are held in combination in the undissociated water molecules.

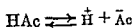
Strength of Acids and Bases

Acids and bases in solution ordinarily do not separate completely into their ions, but contain both molecules and ions. The addition of water to a solution increases the degree of ionization, because more water molecules come between the ions and prevent them from recombining to form undissociated molecules.

Acids that ionize to a large extent in ordinary dilutions are called *strong acids*, while those that ionize to a small extent are called *weak acids*. Strong acids are those that readily furnish a large number of hydrogen ions, while weak acids form relatively few. The ionization equation for the strong acid, hydrochloric acid, may be represented:



in contrast to the ionization equation for the weak acid, acetic acid:



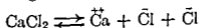
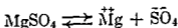
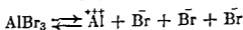
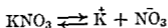
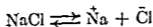
Strong bases are highly ionized and furnish many hydroxyl ions, while *weak bases* are slightly ionized and furnish only a small number of hydroxyl ions. Nearly all salts ionize to a large degree and are not usually spoken of as strong or weak. The degree of ionization of some typical electrolytes in dilute solutions is shown in the following table:

IONIZED PER CENT			IONIZED PER CENT		
Hydrochloric acid	95.0	Sodium hydroxide	91.0
Nitric acid	92.0	Potassium hydroxide	91.0
Sulfuric	61.0	Ammonium hydroxide	...	1.3
Acetic acid	1.3	Potassium chloride	86.0
Carbonic acid	0.17	Sodium chloride	84.0
Boric acid	0.01	Most salts	70-86

As we have just seen, strong and weak electrolytes refer to the degree of ionization. The terms *concentrated* and *dilute* have a meaning different from strong and weak. A concentrated acid or base is one whose solution contains a large amount of the electrolyte compared to the water, while a dilute solution contains a small amount of electrolyte compared to the water. A strong acid or base would cause injury to the tissues if taken internally; however, a weak acid such as acetic, in vinegar, is often used in food, and boric acid may be safely introduced into the tissues of the eye. A weak base such as magnesium hydroxide can be administered to neutralize excess acidity in the stomach.

Salts

The ionization of some typical salts is shown in the following equations:



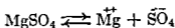
It may readily be seen that no one ion is common to all salts. Since acids, bases, and salts are the only electrolytes, salts may be defined as electrolytes that form neither hydrogen ions nor hydroxyl ions in solution.

Equilibrium In Solution

We have already stated that electrolytes in solution exist as ions and undissociated molecules. These ions and molecules do not remain fixed. There is constant interchange between them because the molecules continuously dissociate to form ions and the ions, as they collide, recombine to form molecules. When the rate of these two reactions is equal, the number of ions and undissociated molecules become constant and the solution is said to have reached a *state of equilibrium*. The changes that occur before an electrolyte in solution reaches equilibrium may be illustrated by the formation of a solution of magnesium sulfate.

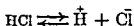
First Stage When the solid MgSO_4 is first added to the water, it exists as undissociated molecules.

Second Stage. As the MgSO_4 dissolves, its molecules dissociate into ions.



When the ions are first formed, they have a large amount of space in which to move about and seldom collide with each other to reform undissociated molecules. The size of the arrow indi-

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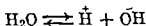


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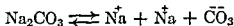
IONIZED PER CENT		IONIZED PER CENT	
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Nitric acid	92.0	Potassium hydroxide ..	91.0
Sulfuric...	61.0	Ammonium hydroxide .	1.3
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Carbonic acid... . .	0.17	Sodium chloride.....	84.0
Boric acid...	0.01	Most salts	70-86

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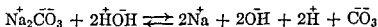
acid solutions. The basic reaction of a solution of sodium carbonate may be understood if we consider what happens when this salt is dissolved in water. Although water is usually considered a nonelectrolyte, a few of its molecules will ionize, forming some hydrogen ions and hydroxyl ions.



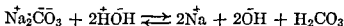
When the salt is dissolved, it ionizes as follows:



Rewriting this equation to include both salt and water, we now have:



It may be observed from the right hand side of the equation that the salt solution is really an equal mixture of sodium hydroxide and carbonic acid. Sodium hydroxide is a strong electrolyte and is almost completely ionized in solution. Carbonic acid, however, is a weak electrolyte since its solution consists mainly of H_2CO_3 molecules and only a few ions. For this reason, a reaction occurs between the hydrogen and carbonate ions forming carbonic acid molecules. A more accurate equation for the solution follows:

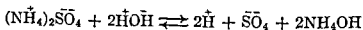


Since the solution now contains an excess of free hydroxyl ions, it acts as a dilute base.

The acidity of an ammonium sulfate solution may be explained in a similar fashion. This salt ionizes when in solution as follows:

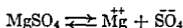


The salt is hydrolyzed by the action of the few hydrogen and hydroxyl ions in water to form an acid and a base.



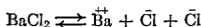
cating the formation of ions is therefore larger than that indicating the formation of molecules.

Third Stage. As the number of ions increases, the chance for collision increases and the rate of formation of molecules increases. When the rate of dissociation of molecules into ions equals the rate of formation of new molecules, a state of equilibrium exists in the solution.

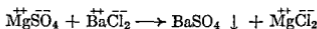


This equilibrium once attained will remain constant as long as the temperature and pressure are not changed. If the temperature is increased, the rate of dissociation and formation of molecules is changed and a new equilibrium is reached.

Other conditions that upset equilibrium are the addition of ions or molecules to the solution or, more important, the removal of these substances from solution. For example, barium chloride ionizes in solution as follows:



If this solution is added to the MgSO_4 solution, the following reaction occurs:



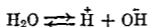
A collision of a barium ion with a sulfate ion results in the formation of a molecule of insoluble barium sulfate which precipitates from the solution. Since this process continually removes barium and sulfate ions from the solution, equilibrium cannot be attained and the reaction proceeds only in the direction of the arrow.

Salts with an Acid or Basic Reaction

It might be expected that solutions of normal salts should be neutral, since they do not contain hydrogen ions or hydroxyl ions. However, certain salts such as sodium carbonate and sodium acetate form solutions that are alkaline, while others such as ammonium sulfate, ammonium chloride, and copper sulfate form

HYDROGEN ION CONCENTRATION

It has already been stated that water ionizes to a very slight extent.



It has been determined that one molecule out of every 550,000,000 molecules of water is ionized. From this fact, it can be calculated that 1 gm. of hydrogen ions is present in 10,000,000 liters of water, or a liter of water contains only $\frac{1}{10,000,000}$ of a gram of hydrogen ions. Since numbers like 10,000,000 are unwieldy, they are often expressed as powers of ten. The powers of ten are usually written as follows:

$10^1 = 10$	$10^5 = 100,000$
$10^2 = 100$	$10^6 = 1,000,000$
$10^3 = 1000$	etc.
$10^4 = 10,000$	

Fractions that contain such large numbers may be expressed as 1 over 10 to a power; or the fraction may be eliminated entirely by taking 10 to the minus power. Examples:

$$\frac{1}{1000} = \frac{1}{10^3} = 10^{-3} \text{ and } \frac{1}{100,000} = \frac{1}{10^5} = 10^{-5}$$

Since a liter of water contains $\frac{1}{10,000,000}$ of a gram of hydrogen ions, the hydrogen ion concentration of water may be expressed as $\frac{1}{10^7}$ or more conveniently as 10^{-7} gm. of hydrogen ions per liter

As the negative power of 10 increases, the hydrogen ion concentration decreases, since the fraction of a gram of hydrogen ions in a liter decreases. There are more hydrogen ions per liter in a solution whose hydrogen ion concentration is 10^{-5} than in one whose concentration is 10^{-6} .

A neutral solution like water has as many hydrogen ions as

In this case, sulfuric acid is a strong acid which remains ionized in solution, while ammonium hydroxide is a weak base that has a tendency to exist in the undissociated form. The hydrogen ions will therefore predominate and the ammonium sulfate solution will be acid in reaction.

The hydrolysis equations are written with double arrows to indicate that the salt being hydrolyzed is formed by the action of the acid and base on the right side of the equation. In general, solutions of normal salts (e. g., sodium carbonate) that are formed from a strong base and a weak acid will have basic properties. Salts (e. g., ammonium sulfate) which have been formed from a strong acid and a weak base have acidic properties when in solution. Normal salts formed from a strong acid and a strong base are not hydrolyzed and thus form neutral solutions.

IMPORTANCE OF IONS

The majority of chemical reactions are between ions rather than between molecules. Electrolytes that ionize in solution react rapidly, nonelectrolytes react slowly in solution, and dry substances usually fail to react with each other. The specific properties of acids, bases, and salts depend upon the ions that are formed when these substances are in solution.

Ions are of fundamental importance in the body. The formation of bones and teeth depends upon the combination of calcium, magnesium, phosphate, and carbonate ions in the proper proportions. Ions in the body fluids produce an osmotic pressure that is responsible for the passage of food and waste material into and out of the tissue cells. Digestion of food in the body is controlled by the ratio of hydrogen ions and hydroxyl ions in the gastric and intestinal fluids. Calcium ions are necessary for the clotting of blood and for the formation of the milk curd in the stomach; ferrous ions are essential in the formation of hemoglobin (the red pigment of the blood). The contraction of muscles and the conveying of impulses by nerves require the presence of certain ions.

method employs an electrically operated electrometer or "pH meter" which indicates the pH of a solution on a special dial. Several types of these pH meters are available and are widely used in industry and in research laboratories. The colorimetric method does not require such expensive equipment, but is not as accurate as the electrometric method. A set of indicators are available that show definite color shades for each pH value. A series of tubes are prepared containing solutions whose pH values vary at regular intervals from pH 0 to pH 14. When the proper indicator is added to each tube the result is a standard series of pH values for use in the colorimetric method. The pH of a solution may be determined by adding one of the indicators to the solution and matching the color that is produced with the color of one of the tubes in the set of permanent color standards.

Importance of pH Values

All body fluids have definite pH values that must be maintained within fairly narrow ranges for proper physiological functions. The pH of the blood is normally between 7.35 and 7.45. Gastric juice has a pH of 1.6 to 1.8 and the urine has a range of pH from 5.5 to 7.0. The saliva is nearly neutral (pH 7), while the bile (pH 7.8-8.6) and the pancreatic juice (pH 8) are more alkaline fluids.

Many biological processes depend on the pH of their environment. The enzymes that digest our food have their optimum activity at definite pH values. Bacteria are best grown on culture media that have had their pH carefully adjusted. The stains that are used to prepare bacteria and tissues for microscopical examination must have the pH of their solutions at a certain value for proper staining technic.

If the pH of the blood falls below 7.0 or goes above 7.8, death occurs. Since many of the reactions that take place in our tissues form acid substances, the blood must have a mechanism to prevent such changes in pH. Certain salts such as bicarbonates, phosphates and salts of proteins have the special function of maintaining the pH of blood and other body fluids within narrow limits. These substances, which are salts of weak acids and are

hydroxyl ions. Since water has a hydrogen ion concentration (abbreviated H^+ conc.) of 10^{-7} , it follows that any solution with a H^+ conc. of 10^{-7} is neutral. A solution is acid when it contains more hydrogen ions than hydroxyl ions. The H^+ conc. of an acid solution would thus be greater than 10^{-7} , or have more than $\frac{1}{10,000,000}$ of a gram of hydrogen ions per liter. For example, a solution with a H^+ conc. of 10^{-3} would have $\frac{1}{1000}$ of a gram of H^+ per liter, or 1 gram of H^+ in 1000 liters. If there are more hydroxyl ions than hydrogen ions in a solution, it is alkaline or basic. Similarly, an alkaline solution would have a H^+ conc. of less than 10^{-7} .

The use of such large fractions or powers is unwieldy, so a simplified method of expressing H^+ conc. was suggested by Sorensen. Since H^+ conc. is usually expressed as 10^{-} some power, he suggested leaving out the 10^{-} and using only the numerical value of the negative power. He called this the *pH value*, meaning the power of the H^+ conc. A neutral solution has a *pH* of 7 since its H^+ conc. is 10^{-7} . The *pH* of alkaline solutions is greater than 7, while the *pH* of acid solutions is less than 7. The relationship between the H^+ conc. of a solution and its *pH* is shown in the following diagram:

	Acid						Neutral				Base					
H^+ conc.	10^0	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}	10^{-8}	10^{-9}	10^{-10}	10^{-11}	10^{-12}	10^{-13}	10^{-14}	
<i>pH</i>	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
	\uparrow 0.1 M HCl		\uparrow 0.1 M Acetic Acid			\uparrow 0.1 M H_2BO_3	\uparrow Neutral Solution		\uparrow 0.1 M NH_4OH			\uparrow 0.1 M NaOH				

The methods for determining the *pH* of a solution may be classified as electrometric or colorimetric. The electrometric

method employs an electrically operated electrometer or "pH meter" which indicates the pH of a solution on a special dial. Several types of these pH meters are available and are widely used in industry and in research laboratories. The colorimetric method does not require such expensive equipment, but is not as accurate as the electrometric method. A set of indicators are available that show definite color shades for each pH value. A series of tubes are prepared containing solutions whose pH values vary at regular intervals from pH 0 to pH 14. When the proper indicator is added to each tube the result is a standard series of pH values for use in the colorimetric method. The pH of a solution may be determined by adding one of the indicators to the solution and matching the color that is produced with the color of one of the tubes in the set of permanent color standards.

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able to withstand additions of acid or alkali without appreciable change in pH , are called *buffers*. The specific role they play in maintaining a constant pH in the blood will be discussed under acid-base balance in the chapter on blood. (See Chapter XX).

Buffer salts have many important applications in physiological studies and are often used to maintain the pH of biological solutions.

REVIEW QUESTIONS

1. Define and give examples of conductors, insulators, electrolytes, and nonelectrolytes.
2. How does a solution of an electrolyte conduct an electric current from electrodes A to B in Figure 32?
3. Outline the important principles of the theory of ionization.
4. Give definitions of acids, bases, and salts from the standpoint of ionization.
5. Why are some acids and bases referred to as strong acids or bases, whereas others are termed weak acids or bases? Give an example of a strong acid, a strong base, a weak acid and a weak base.
6. Write the equations for the ionization of the following salts in aqueous solutions: (a) sodium sulfate (b) ammonium phosphate and (c) aluminum carbonate. How can the ionization of salts be readily distinguished from the ionization of acids or bases?
7. Explain the steps in the ionization of sodium nitrate when it is dissolved in water, to form a solution in which there is equilibrium between the ions and the undissociated molecules.
8. Why is a solution of ammonium chloride acid in reaction, while a solution of sodium borate is alkaline in reaction?
9. A certain acid solution contains 1×10^{-5} of a gram of hydrogen ions in a liter. In what other ways could you express the hydrogen ion concentration of the solution? What is its pH ?
10. Construct a diagram of the pH scale similar to that on page 102 in which the acids and bases below the scale are replaced by physiological fluids at their proper pH positions.
11. Why are pH values widely used to designate the acidity or alkalinity of biological fluids?
12. How do you explain the fact that water is a neutral solution?
13. What is a buffer? What would happen to the body if no buffers were present in the blood or tissues?

CHAPTER X

Introduction to Organic Chemistry

UNTIL early in the nineteenth century, a sharp distinction was made between organic and inorganic compounds. The chemists believed that organic compounds were made only in the living cells or organs of plants and animals. The only compounds that could be synthesized in the laboratory were the inorganic or "lifeless" compounds. In 1828, Wöhler, a German chemist, prepared urea by heating a mixture of two inorganic compounds, potassium cyanate and ammonium sulfate. Urea was considered an organic substance because it was produced by the body and was found in the blood and urine. This discovery that organic compounds could also be synthesized in the laboratory materially affected the progress of organic chemistry. Since 1828, thousands of the compounds present in plants and animals have been made in the laboratory by the chemist.

Since Wohler's experiment disproved the belief that organic compounds could be made only by living cells, a new classification of chemical compounds was necessary. It was known that the majority of compounds made by plants and animals contained the element carbon. We now classify organic compounds as those that contain carbon as one of their elements. Therefore, *organic chemistry* is a study of the compounds of carbon, regardless of their relation to the living cell. Compounds that do not contain carbon are considered as inorganic compounds and are studied in inorganic chemistry. A few carbon compounds had previously been classed as inorganic, such as carbon dioxide,

carbon monoxide, carbonic acid, and the carbonates. For convenience, their classification has remained the same and they are studied as part of inorganic chemistry. Organic compounds are much more numerous than inorganic compounds. There are



Fig. 33. Artificial hand and arm made of plastic material. Plastics are synthetic organic compounds that have many medical and industrial applications. (From *Modern Plastics*, 26:142.)

nearly 500,000 known organic compounds compared to about 25,000 inorganic.

Organic substances are found in all types of plant and animal tissues. Foods containing carbohydrates, fats, and proteins are organic in nature and are obtained from edible plants and animal

tissue. Drugs, alcohol, vitamins, hormones, and many other compounds that are used in medicine are prepared from the tissues of plants or animals. Coal, coke, natural gas, and petroleum and its derivatives (gasoline, lubricating oils, kerosene, petroleum jelly, etc.) have as their source products of plants and animals that lived many thousand years ago.

IMPORTANCE OF ORGANIC COMPOUNDS

Our tissues are composed of organic substances and depend on a supply of carbon compounds for their continued existence. To maintain the health of the body, we require an adequate supply of food, vitamins, hormones, enzymes, and many other organic compounds. The majority of drugs that are used for their beneficial physiological effects are organic in nature.

The textile fabrics that are commonly used are either naturally occurring organic material like wool, cotton, silk, and linen, or synthetic organic compounds like rayon and nylon. Perfumes, dyes, cellophane, aviation gasoline, lacquers, bakelite, synthetic vitamins, plastics, and the sulfa drugs are but a few of the organic chemists' contributions to our welfare.

COMPARISON OF ORGANIC AND INORGANIC COMPOUNDS

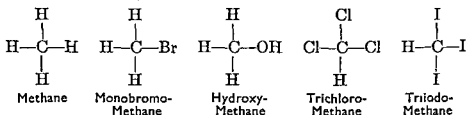
As stated previously, the number of organic compounds is far greater than the number of inorganic compounds. Any of the 96 elements may combine to form inorganic substances, while organic compounds are composed mainly of carbon, hydrogen, and oxygen with occasional nitrogen, sulfur, and phosphorus. Organic molecules are usually more complex and therefore possess a higher molecular weight than inorganic molecules. Proteins, for example, are organic molecules with molecular weights that range from several thousand to over a million.

Inorganic compounds usually ionize in solution and therefore react rapidly with other compounds. Organic substances are non-electrolytes and ionize slowly or not at all. Reactions between organic compounds are slow, since they represent the activity of molecules rather than ions. Catalysts are particularly useful for increasing the rate of the organic reactions that occur in the body.

Inorganic compounds whose molecules have the same composition usually have the same properties. The molecular or *empirical* formula NaOH represents only sodium hydroxide and all molecules of NaOH have the same properties. However, organic compounds that possess different properties may often have the same empirical formula. The formula for glucose, the sugar present in the blood, is $C_6H_{12}O_6$. Fifteen other sugars including fructose and galactose have this empirical formula; yet they vary in solubility, degree of sweetness, and utilization by the animal body. These compounds are called *isomers* and the different properties of each one is due to the arrangement of the atoms within the molecule.

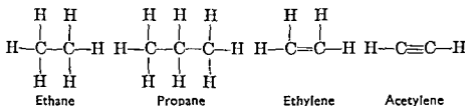
THE PROPERTIES OF CARBON

The carbon atom has a valence of 4 and is therefore able to unite with 4 atoms or radicals that have a valence of 1. The organic molecule composed of carbon combined with 4 hydrogen atoms is the simplest organic compound known and is called methane. The formulas for methane and other simple carbon compounds are represented as follows:



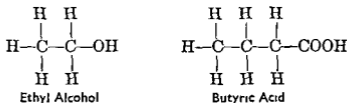
Formulas written in this manner are called *structural formulas* since they indicate the way the atoms are linked together to form the molecule. Since carbon does not ionize, its bonds of valence may be joined to atoms with a positive valence (as H, above) or a negative valence (as Br, OH, Cl, and I).

Carbon atoms also possess the unique ability to unite with each other to form a large number of complex molecules. They are ordinarily linked to each other by only one of their valence bonds, but may use two or three of these bonds in this carbon to carbon linkage.

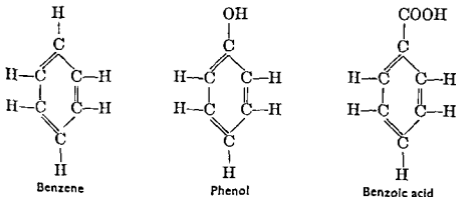


DIVISIONS OF ORGANIC COMPOUNDS

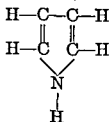
Organic molecules usually consist of either a chain of carbon atoms or a ring of carbon atoms. An organic compound that is composed of a chain of carbon atoms containing other atoms and radicals is called an *aliphatic compound*:



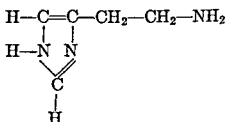
Those compounds which consist of a ring of atoms are called *cyclic compounds*. If the ring of a cyclic compound is composed entirely of carbon atoms, it is called a *carbocyclic compound*; if atoms other than carbon are also present in the ring, the compound is *heterocyclic*. The most common carbocyclic compound is benzene; this substance and its derivatives are often called *aromatic compounds* because of their aromatic odor. The formulas of benzene and two of its derivatives illustrate carbocyclic compounds:



The following are examples of heterocyclic compounds containing nitrogen in the ring:



Pyrrole



Histamine

The two major divisions of organic chemistry are, therefore, aliphatic and cyclic. There are many types of aliphatic and cyclic compounds that will be considered in the following chapters. A classification of these compounds may aid in the simplification of their study:

ALIPHATIC COMPOUNDS

Hydrocarbons
Alcohols
Aldehydes
Ketones
Ethers
Acids
Esters
Amines

CYCLIC COMPOUNDS

A. Carbocyclic
Hydrocarbons
Alcohols
Aldehydes
Ketones
Ethers
Acids
Esters
Amines
B. Heterocyclic

REVIEW QUESTIONS

1. Why was the synthesis of urea by Wohler in 1828 important to the progress of organic chemistry?
2. Of what importance is organic chemistry in the practice of medicine?
3. List several of the outstanding differences between organic and inorganic compounds.
4. Compare the meaning of the terms: empirical formula, isomers, and structural formula.
5. Define aliphatic, cyclic, carbocyclic, heterocyclic, and aromatic.

CHAPTER XI

Aliphatic Compounds

THE simplest aliphatic compounds are known as hydrocarbons since they consist of only hydrogen and carbon. Many aliphatic compounds, however, contain oxygen in addition to hydrogen and carbon. The addition of this element greatly increases the number and complexity of organic compounds. Since there are over 500,000 known compounds of carbon it would at first seem an impossible task to master the fundamentals of organic chemistry. However, as seen on page 110, these substances can be grouped into a few fundamental classes, or series, whose members possess similar properties. Organic compounds are characterized by the presence of certain active groups or radicals which determine the chemical behavior of the compound. Formulas of organic compounds are usually written in such a way that the active group or radical is emphasized. All of the members of each class of compounds show properties that are characteristic of their group, and vary only in degree as the size of the molecule changes.

A knowledge of the characteristic or key group of the major classes of aliphatic compounds will be very helpful in understanding the chemical reactions and properties of any organic compound.

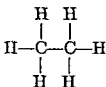
Some of the important members of these classes of aliphatic compounds will be considered in this chapter.

HYDROCARBONS

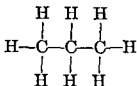
Organic compounds which consist of only hydrogen and carbon are called *hydrocarbons*. Methane, the simplest hydrocarbon, is the lowest member in a series of aliphatic hydrocarbons.



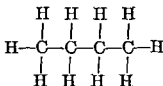
Methane



Ethane



Propane



Butane

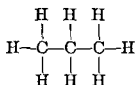
Each successive member of the series contains 1 more carbon atom and 2 more hydrogen atoms than the one preceding it. As the members of the series increase in size by the addition of CH_2 , several common substances are encountered. For example, natural gas is a mixture of the first four members (CH_4 to C_4H_{10}), gasoline is a mixture of hydrocarbons with 5 to 10 carbons, mineral and lubricating oils contain 14 to 24 carbons, and paraffin is a mixture of members with 22 to 30 carbon atoms per molecule. This group is called the *methane series* after the name of its first member; or the *paraffin series* because paraffin is a mixture of the higher members.

Crude petroleum, the best natural source of hydrocarbons, consists of a mixture of these compounds containing from 1 to 60 carbon atoms. Petroleum is distilled commercially to produce gasoline, kerosene, mineral oil, lubricating oil, petroleum jelly, paraffin, and other useful compounds.

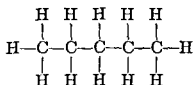
Many of the lower members of this series are inflammable; in burning, they readily combine with oxygen, forming carbon dioxide and water. Natural gas burns readily and is used as a source of heat. Gasoline burns with explosive violence when mixed with air. The force generated by this explosion is used as power to drive gasoline motors. Kerosene burns with a yellow-white flame and is used for illumination in lamps and lanterns. Another distillation product from petroleum, known as fuel oil, is finding increased usage in home heating.

SATURATED AND UNSATURATED
ALIPHATIC COMPOUNDS

The hydrocarbons of the methane series are said to be *saturated* because the carbon atoms have combined with all the hydrogen atoms they are capable of holding.



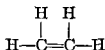
Propane



Pentane

Saturated hydrocarbons have only *single bonds between the carbon atoms*.

An organic compound is called *unsaturated* when any of its carbon atoms are not completely saturated with hydrogen atoms. Unsaturated compounds, therefore, have *double or triple bonds between the carbon atoms*. A series of hydrocarbons similar to the methane series are formed by these unsaturated compounds. Hydrocarbons that have a double bond between the first two carbon atoms form the *ethylene series*, those with a triple bond between the first two carbon atoms compose the *acetylene series*. The first member of each series is shown below.

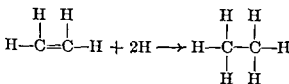


Ethylene



Acetylene

This type of compound is more active chemically than the saturated compounds because they are able to unite with other atoms or radicals. If 2 atoms of hydrogen combined with ethylene, the saturated compound, ethane, would be formed.



Ethylene

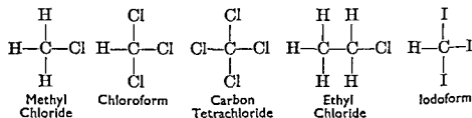
Ethane

In a similar fashion, the addition of 4 atoms of hydrogen would "saturate" the acetylene molecule to form ethane.

Ethylene exists as a gas and is used in medicine as an anesthetic. Acetylene gas is widely used in industry in combination with oxygen in oxyacetylene torches. The intense heat produced by the oxyacetylene flame will melt iron and steel, therefore it is used in cutting and welding processes.

HALOGEN DERIVATIVES OF HYDROCARBONS

Chlorine, bromine, and iodine belong to a group of chemically similar elements called *halogens*. These elements are very active chemically and react with the hydrocarbons, replacing hydrogen atoms in their molecules.



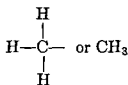
The halogen derivatives illustrated above are frequently used in medicine and industry. Methyl and ethyl chlorides exist as liquids at high pressures. They are refrigerants since they vaporize readily and draw heat from other objects. When sprayed on the skin, they produce local anesthesia by freezing the nerve endings. Chloroform is a volatile liquid that was once widely used as an anesthetic. It sometimes produces harmful effects, however, and has been replaced by other anesthetics. Carbon tetrachloride is used in medicine to kill or stupefy hookworms in the intestinal tract so they can be removed by the use of a cathartic. Both chloroform and carbon tetrachloride are nonflammable and are good solvents for fats and grease. Large quantities of carbon tetrachloride are used in dry cleaning and in the "pyrene" type of fire extinguisher. Iodoform has some anesthetic properties but it is seldom used, and its chief use is as an antiseptic.

HYDROCARBON RADICAL

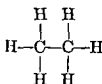
A hydrocarbon from which a hydrogen atom has been removed leaving an unattached valence bond is called a *hydrocarbon radical*. The methyl and ethyl radicals may be represented as follows:



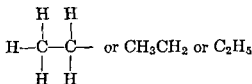
Methane



Methyl Radical



Ethane



Ethyl Radical

Such radicals have a valence of 1 or may be considered to have 1 free bond that can be attached to an atom or radical with a valence of 1. Methyl chloride, CH_3Cl , and ethyl chloride, $\text{CH}_3\text{CH}_2\text{Cl}$, would represent a methyl and ethyl radical combined with a chloride radical.

Within each class of aliphatic compounds, there are a series of compounds based on methane, ethane, propane and higher members of the series:

HYDROCARBON	ALCOHOL	ALDEHYDE	ACID, ETC.
Methane, CH_4	CH_3OH	HCHO	HCOOH
Ethane, C_2H_6	$\text{C}_2\text{H}_5\text{OH}$	CH_3CHO	CH_3COOH
Propane, C_3H_8	$\text{C}_3\text{H}_7\text{OH}$	$\text{C}_2\text{H}_5\text{CHO}$	$\text{C}_2\text{H}_5\text{COOH}$
etc.	etc.	etc.	etc.

ALCOHOLS

If one or more of the hydrogen atoms of a hydrocarbon are replaced by a hydroxyl group, the resulting compound is called an *alcohol*.



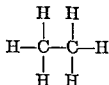
Methane
 CH_4



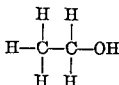
Methyl Alcohol
 CH_3OH



Alcohol Group

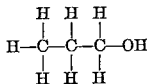


Ethane
 C_2H_6

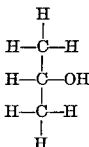


Ethyl Alcohol
 $\text{C}_2\text{H}_5\text{OH}$

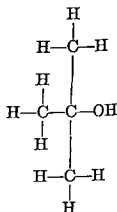
An alcohol in which the OH group is linked to an end carbon is called a *primary alcohol*. If the OH group is attached to a carbon atom within the chain, that is, a carbon atom which is linked to two other carbon atoms, the compound is called a *secondary alcohol*. A *tertiary alcohol* contains an OH group attached to a carbon atom that is linked to three other carbon atoms.



Primary
Propyl Alcohol
 $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$



Secondary
Propyl Alcohol
 $\text{CH}_3\text{CHOHCH}_3$

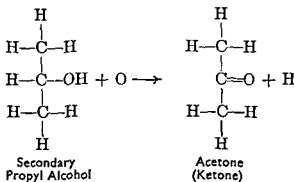
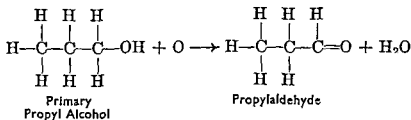


Tertiary
Butyl Alcohol
 $(\text{CH}_3)_3\text{COH}$

Reactions of Alcohols

The oxidation of an alcohol to form new compounds is one of the most important reactions involving alcohols. The rapid

oxidation or burning of alcohols results in complete oxidation to form carbon dioxide and water. When methyl or ethyl alcohol are burned, they yield considerable amounts of energy (heat). If alcohols are treated with oxidizing agents at lower temperatures, they form several intermediate compounds (aldehydes, ketones, organic acids, etc.) before being completely oxidized to carbon dioxide and water. Mild oxidation of a primary alcohol results in the formation of an *aldehyde*, while a similar oxidation of a secondary alcohol produces a *ketone*.



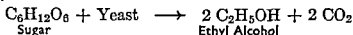
Oxygen is represented as O instead of O₂ in the above equations because it is released from oxidizing agents in the form of atoms. This atomic oxygen, often called *nascent oxygen*, is very active and reacts rapidly with compounds before it has an opportunity to combine to form molecular O₂.

Another common reaction of alcohols is their reaction with acids, in which they behave in a manner similar to inorganic hydroxides. When an acid reacts with an alcohol, water and an organic ester are formed; when an acid reacts with an inorganic hydroxide, water and a salt are formed. Alcohols do not ionize and therefore do not contain the hydroxyl ions which are responsible for many of the properties of inorganic hydroxides.

Important Alcohols

Methyl alcohol, CH_3OH , is commonly called wood alcohol because it is often made by the destructive distillation of wood. It is a colorless, volatile liquid; in the crude state it has a disagreeable odor. It burns readily and may be used as fuel in alcohol lamps and in certain engines. Methyl alcohol is not completely oxidized in the body but forms formic acid which may first cause blindness and then death. Since it is used as a solvent for shellac in the varnish industry, the workmen must be protected from its fumes.

Ethyl alcohol, $\text{C}_2\text{H}_5\text{OH}$, is also known as grain alcohol since it may be made by fermentation of various grains. It is prepared commercially by the fermentation of the sugars and starch of common grains such as corn and barley. Yeast contains enzymes that catalyze the fermentation of sugars to alcohol and carbon dioxide.



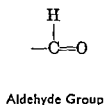
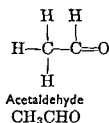
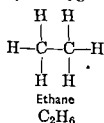
The process of fermentation also produces the alcohol found in wines and liquors. When ethyl alcohol is taken internally, it is rapidly absorbed and oxidized. It may therefore be used as a readily available source of energy and is often employed to overcome shock or collapse. If large quantities are taken, it causes depression of the higher nerve centers, mental confusion, lack of muscular coordination, lowering of normal inhibitions, and eventually results in stupor.

Ethyl alcohol is a colorless, volatile liquid with a pleasant odor and a burning taste. It is an excellent solvent for many medicines, flavoring extracts, and perfumes. A 70 per cent solution has slightly antiseptic properties and is often used to sterilize the skin for minor surgical procedures. Rubbing alcohol and alcohol that is used commercially is rendered unfit for beverage purposes (denatured) by the addition of methyl alcohol, formaldehyde, phenol, acetone, and other toxic substances. Large quantities of ethyl alcohol are used in the manufacture of ether, chloroform, ethylene, iodoform, and other important organic compounds.

Glycerol, $\text{CH}_2\text{OH}-\text{CHOH}-\text{CH}_2\text{OH}$, is a common trihydric alcohol and is sometimes called glycerin. It is prepared by the hydrolysis of fats, which are esters of fatty acids and glycerol. It is a syrupy liquid that is soluble in all proportions in water and alcohol. Glycerol has the ability to take up moisture from the air; when applied in the form of cosmetics and hand lotions, it tends to keep the skin soft and moist. Since glycerol is readily converted into nitroglycerin, which is a common explosive, the demand for glycerol increases in time of war. Waste fats and oils may serve as an additional source of glycerol in an emergency.

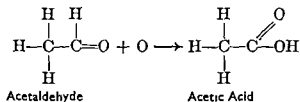
ALDEHYDES

An *aldehyde* is a derivative of a hydrocarbon in which two of the hydrogen atoms on an end carbon atom have been replaced by an oxygen atom.



Oxidation of Aldehydes

Although aldehydes are formed by oxidation, they may be oxidized further to form organic acids. The oxidation occurs readily and may be represented as follows:



Since aldehydes are easily oxidized, they have an affinity for oxygen and are good reducing agents. Simple sugars contain the aldehyde group and will reduce cupric ions ($\overset{++}{\text{Cu}}$) to cuprous ($\overset{+}{\text{Cu}}$). The cuprous ions then form cuprous oxide, which settles out of

the solution as a red precipitate. This reaction is the basis of Benedict's test, a clinical method of determining sugar in urine.

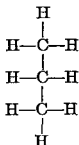
Important Aldehydes

Formaldehyde, $\text{H}-\text{CHO}$, is readily prepared by the oxidation of methyl alcohol. It is a gas with a sharp penetrating odor. The gas dissolves readily in water and a 40 per cent solution is known as *formalin*. Formalin is widely used as a disinfectant and as a preservative of tissues. *Paraformaldehyde* is formed by the union or polymerization of several molecules of formaldehyde, a process that is common to all aldehydes. The white solid that is formed is used as an antiseptic.

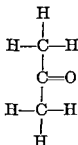
Acetaldehyde, CH_3-CHO , is a colorless liquid with a characteristic odor. Three molecules of acetaldehyde polymerize to form paraldehyde which is an effective hypnotic, used to produce sleep. Since this compound has an irritating odor and an unpleasant taste, it is usually administered by rectum.

KETONES

A *ketone* is a hydrocarbon derivative in which two of the hydrogen atoms on a carbon atom not at the end of the chain are replaced by an oxygen atom.



Propane
 C_3H_8



Acetone
 $\text{CH}_3-\text{CO}-\text{CH}_3$



Ketone Group

As we have already seen, aldehydes are formed by the oxidation of primary, and ketones by the oxidation of secondary alcohols.

Oxidation of Ketones

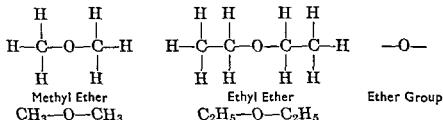
Ketones may be oxidized to form organic acids; however, they are more difficult to oxidize than aldehydes.

Important Ketones

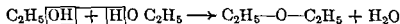
Acetone, $\text{CH}_3\text{—CO—CH}_3$, is a colorless, volatile liquid with a pleasant odor. In diabetes mellitus, abnormally large amounts of acetone are found in the blood and urine. Acetone is used commercially as a solvent for many organic compounds and is used in the manufacture of chloroform.

ETHERS

Ethers are organic oxides, formed by the union of 2 hydrocarbon radicals with an atom of oxygen.



Ethers are prepared by the dehydration of alcohols. Sulfuric acid, an effective dehydrating agent, readily removes a molecule of water from two molecules of ethyl alcohol to produce ethyl ether.



The most commonly known ether is *ethyl ether* which is extensively used as a general anesthetic (Fig. 34). It is easy to administer and causes excellent relaxation of the muscles. The blood pressure, the pulse rate, and the rate of respiration as a rule are only slightly affected. Its main disadvantages are its irritating effect upon the respiratory passages and its nauseating after-effects. Much care must be exercised in the use of ether in the hospital because of its extreme inflammability; serious fires and explosions have occurred from the careless use of this anesthetic.

the solution as a red precipitate. This reaction is the basis of Benedict's test, a clinical method of determining sugar in urine.

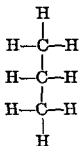
Important Aldehydes

Formaldehyde, $\text{H}-\text{CHO}$, is readily prepared by the oxidation of methyl alcohol. It is a gas with a sharp penetrating odor. The gas dissolves readily in water and a 40 per cent solution is known as *formalin*. Formalin is widely used as a disinfectant and as a preservative of tissues. *Paraformaldehyde* is formed by the union or polymerization of several molecules of formaldehyde, a process that is common to all aldehydes. The white solid that is formed is used as an antiseptic.

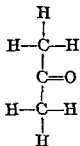
Acetaldehyde, CH_3-CHO , is a colorless liquid with a characteristic odor. Three molecules of acetaldehyde polymerize to form paraldehyde which is an effective hypnotic, used to produce sleep. Since this compound has an irritating odor and an unpleasant taste, it is usually administered by rectum.

KETONES

A *ketone* is a hydrocarbon derivative in which two of the hydrogen atoms on a carbon atom not at the end of the chain are replaced by an oxygen atom.



Propane
 C_3H_8



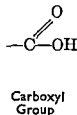
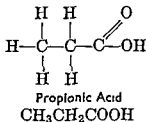
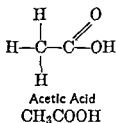
Acetone
 $\text{CH}_3-\text{CO}-\text{CH}_3$



Ketone Group

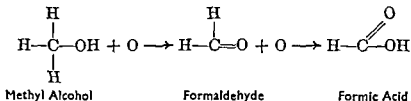
As we have already seen, aldehydes are formed by the oxidation of primary, and ketones by the oxidation of secondary alcohols.

characteristic acid group. This group is structurally written $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{OH} \end{array}$ or, more simply, $-\text{COOH}$, and is called the *carboxyl* group.



The hydrogen of the carboxyl group forms hydrogen ions when the acid is dissolved in water. Organic acids, therefore, have all the common characteristics of an inorganic acid. They turn blue litmus red, have a sour taste, and exhibit reactions characteristic of all acids. In general, they are weak acids because they ionize only slightly in solution.

Organic acids are formed by the oxidation of an aldehyde or ketone. We have already stated that the oxidation of a primary alcohol results in the formation of an aldehyde and that the further oxidation of the aldehyde forms an organic acid.



Common organic acids such as formic and acetic acids which contain one *carboxyl* group are called *monobasic* acids. *Dibasic* acids contain two, and *tribasic* acids, three carboxyl groups. Oxalic acid, $\text{COOH}-\text{COOH}$, is an example of a dibasic acid, while citric acid, $\text{CH}_2-\text{COOH}-\text{COH}-\text{COOH}-\text{CH}_2-\text{COOH}$, is tribasic. Many organic acids contain hydroxyl groups in addition to the OH of the carboxyl group and are classified as *hydroxy acids*. Lactic acid, $\text{CH}_3-\text{CHOH}-\text{COOH}$, tartaric acid,

Recently, divinyl ether, $\text{CH}_2=\text{CH}-\text{O}-\text{CH}=\text{CH}_2$, which is called vinethene has been used as a rapid acting, short term anesthetic replacing the more dangerous chloroform. This anesthetic is ideal for bone-setting and minor surgery in children and, if properly administered, does not produce nausea and vomiting.



Fig. 34. The clinical application of ethyl ether in anesthesia. (From Cole, W. H., and Elman, R.: Textbook of General Surgery, New York, Appleton-Century-Crofts, Inc.)

Ethers in general are good solvents for fats, oils, gums, and resins. They are often used in the laboratory for the extraction of fats from foods and animal tissues.

ORGANIC ACIDS

An *organic acid* is a derivative of a hydrocarbon in which one or more of the hydrogen atoms have been replaced by the

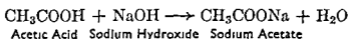
lactic acid is formed by the tissues; therefore, it occurs as a normal constituent of the blood. The calcium salt of this acid is sometimes used in medicine to supplement the calcium of the diet.

Oxalic acid, $\text{COOH}-\text{COOH}$, occurs as a salt in the leaves of certain vegetables and is one of the strongest naturally occurring acids. It is used to bleach straw and to remove stains on fabrics, porcelain, and metals. It is especially useful for removing potassium permanganate stains from the skin.

Citric acid, $\text{CH}_2-\text{COOH}-\text{COH}-\text{COOH}-\text{CH}_2-\text{COOH}$, is a normal constituent of citrus fruits. It is frequently employed to impart a sour taste to food products and beverages. The sodium salt is used to prevent the clotting of blood, the magnesium salt is a mild laxative.

ORGANIC SALTS

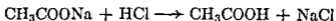
When an organic acid reacts with an inorganic base, an *organic salt* is formed:



Organic salts are similar to inorganic salts in that they ionize in solution:



When an organic salt is treated with an inorganic acid, the inorganic salt is formed and the organic acid is set free:



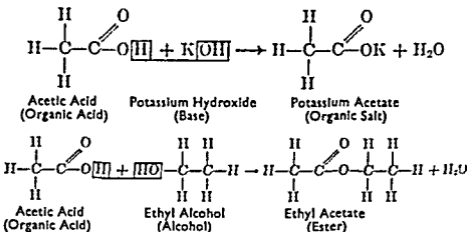
Typical Organic Salts

Lead acetate, sometimes called sugar of lead, is used externally to treat poison ivy and certain skin diseases. Commercially it is used in large quantities in the manufacture of white lead paints. Paris green is a complex salt that contains copper acetate and is used as an insecticide. A dilute solution of aluminum

$\text{COOH}-\text{CHOH}-\text{CHOH}-\text{COOH}$, and citric acid are common examples of hydroxy acids.

Reactions of Organic Acids

A characteristic property of organic acids is their ability to react with inorganic hydroxides (bases) to form *organic salts* and with organic hydroxides (alcohols) to form *esters*.



Important Organic Acids

Formic acid, $\text{H}-\text{COOH}$, is a colorless liquid with a sharp, irritating odor. This acid is found in the sting of ants, bees, and other insects. The sting or bite of an insect is often treated with a weak alkali such as baking soda or household ammonia to neutralize the formic acid.

Acetic acid, CH_3-COOH , is formed by the oxidation of ethyl alcohol when cider or molasses are fermented to make vinegar. Vinegar contains about 4 per cent acetic acid. Pure acetic acid is produced by the distillation of wood and is a white crystalline solid called *glacial acetic acid*. Commercially acetic acid is used as a solvent in the preparation of cellophane, acetone, white lead paint, and photographic films.

Lactic acid, $\text{CH}_3-\text{CHOH}-\text{COOH}$, is a colorless liquid that is formed when lactose (milk sugar) is fermented by certain bacteria. The taste of sour milk and buttermilk is due to the presence of lactic acid. In the process of muscular contraction,

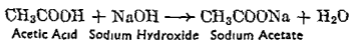
lactic acid is formed by the tissues; therefore, it occurs as a normal constituent of the blood. The calcium salt of this acid is sometimes used in medicine to supplement the calcium of the diet.

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ORGANIC SALTS

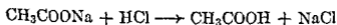
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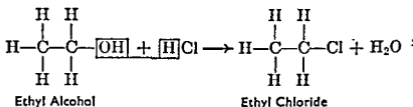
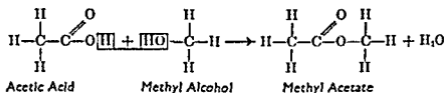
Lead acetate, sometimes called sugar of lead, is used externally to treat poison ivy and certain skin diseases. Commercially it is used in large quantities in the manufacture of white lead paints. Paris green is a complex salt that contains copper acetate and is used as an insecticide. A dilute solution of aluminum

acetate called Burow's solution is employed in the treatment of skin diseases.

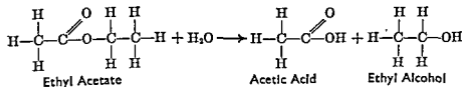
Salts of the hydroxy organic acids are often used in medicine. Calcium lactate and ferric ammonium citrate may be used to supply additional calcium or iron in the diet. Magnesium citrate and Rochelle salt (sodium potassium tartrate) are saline cathartics. Since tartaric acid contains two carboxyl groups, double salts like Rochelle salt are possible. Tartar emetic is another double salt of tartaric acid (potassium antimony tartrate).

ESTERS

The compound formed in the reaction between an acid and an alcohol is called an *ester*. Esters may be formed by the reaction of either organic or inorganic acids with alcohols.



Esters differ from organic salts in that they do not ionize in water solution. Therefore they react very slowly with other compounds unless a catalyst is present. One of their most important reactions is hydrolysis, i. e., reaction with water to form an acid and an alcohol:



Esters are widely distributed in nature and are responsible for the odor of most fruits and flowers. The characteristic tastes and odors of the different esters find application in the manufacture of artificial flavoring extracts and perfumes. Synthetic esters that are commonly used as food flavors are amyl acetate for banana, octyl acetate for orange, ethyl butyrate for pineapple, amyl butyrate for apricot, and ethyl formate for rum.

Other esters are commonly used for medicinal purposes. The use of methyl and ethyl chlorides as local anesthetics has already been discussed. Ethyl acetate is applied externally in the treatment of skin diseases caused by parasites. Ethyl nitrite, which is commonly called sweet spirits of niter, is a diuretic and is used for lowering fevers in children. Amyl nitrite is used to lower blood pressure temporarily, and causes relaxation of muscular spasms (as in angina pectoris and asthma). Glycerol trinitrate or nitro glycerin is a vasodilator that is administered in certain cases of heart attack. It is used industrially as a powerful explosive; dynamite is nitroglycerin mixed with sawdust for convenience in handling.

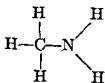
AMINES

Amines are organic derivatives of ammonia, in which one or more of the hydrogen atoms have been replaced by an organic radical. The characteristic group present in amines is called the

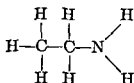
amino group and is written: $\begin{array}{c} \text{H} \\ \diagup \\ \text{N} \\ \diagdown \\ \text{H} \end{array}$ or NH_2 .



Ammonia



Methyl Amine



Ethyl Amine

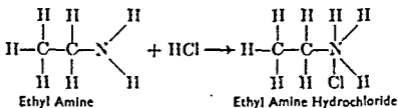


Amino Group

Primary amines like those shown above, in which 1 H atom of ammonia is replaced by an organic radical, are the most

common amines. There are other amines in which 2 or 3 H atoms of ammonia are replaced, called *secondary amines* and *tertiary amines* respectively.

A characteristic property of amines is their ability to react with inorganic acids.



When foods rich in protein, such as meat and fish, are decomposed by bacteria, amines called *ptomaines* are formed. These ptomaines are formed in the large intestine in the process of *putrefaction* and are also present in spoiled foods. When ptomaines are present in the intestine they enter the blood stream and are carried to the liver. There they are changed into harmless substances which are excreted in the urine. Ptomaine poisoning caused from eating spoiled foods is usually due to pathogenic bacteria in the food or to toxic substances produced within the bacteria, rather than by ptomaines.

Chemically related to the amines are *amino acids* which contain an amino group and a carboxyl group. Amino acids are the fundamental units in the protein molecule and will be discussed under proteins.

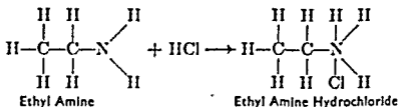
REVIEW QUESTIONS

1. Why is a knowledge of the characteristic group of a class of organic compounds important?
2. Write the formula for an aliphatic hydrocarbon that contains 8 carbon atoms. How would you name the compound? What relation does this compound have to commercial gasoline?
3. What effect would the exhaustion of all petroleum supplies have on the progress of a nation at war, and at peace?
4. Write the formula for a saturated aliphatic compound and an unsaturated compound. How is unsaturation indicated in the formula of a compound?
5. What is meant by the expression, "to saturate an unsaturated organic compound"?

6. Write the structural formulas for two halogen derivatives of hydrocarbons. Compare chloroform and carbon tetrachloride as to their usefulness in medicine and in industry.
7. How would you characterize a hydrocarbon radical? Give two examples of such radicals.
8. Explain the difference between a primary, a secondary, and a tertiary alcohol. Give an example of each of the three alcohols.
9. Write an equation for the oxidation of primary butyl alcohol. What products are usually formed on complete oxidation of an alcohol?
10. What is your conception of nascent oxygen?
11. In what ways are alcohols similar to inorganic bases? In what ways do they differ?
12. Why is methyl alcohol poisonous when taken internally?
13. List several important uses for ethyl alcohol.
14. What is meant by denatured alcohol? Why is denatured alcohol frequently used in the hospital and in industry?
15. How might nitroglycerin be prepared? Why is nitroglycerin especially important in time of war?
16. Write the formula for an aldehyde other than acetaldehyde. Circle the characteristic group in the compound.
17. Why are aldehydes good reducing agents? How is this reducing property applied to the determination of sugar in the urine?
18. Name and write the formula for a common ketone. Where do we often encounter ketones in the practice of medicine?
19. Upon what principle is the preparation of ethyl ether based? Explain.
20. List the advantages and disadvantages of the use of ethyl ether as an anesthetic.
21. Compare the properties and reactions of organic and inorganic acids.
22. Starting with propyl alcohol, show the steps involved in the oxidation of this compound to form propionic acid.
23. Differentiate between the following terms: monobasic, dibasic, tribasic, and hydroxy acids. Give an example of each.
24. List five important uses of organic acids in medicine.
25. Write an equation for the formation of a typical organic salt.
26. What organic salts are often used to supplement the calcium or iron content of the diet? Which are used as cathartics?
27. What is an organic ester? Write the formula for the ester that is formed by the reaction of propionic acid and propyl alcohol. How would you name this compound?
28. List several medical uses of esters.
29. Give an example of an amine. Would this compound be acidic or basic in reaction? Why?
30. What are ptomaines? Are ptomaines responsible for ptomaine poisoning? Explain.

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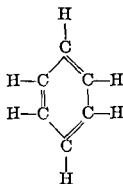
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4. Write the formula for a saturated aliphatic compound and an unsaturated compound. How is unsaturation indicated in the formula of a compound?
5. What is meant by the expression, "to saturate an unsaturated organic compound"?

erties, however, more closely resemble those of a saturated hydrocarbon. For many years chemists were unable to decide on a structural formula that would account for the reactions and properties of benzene. In 1865, Kekule proposed a ring structure for benzene which is generally accepted today. The structural formula for benzene was represented as 6 carbons combined in the form of a hexagon with alternate single and double bonds:



The alternate double bonds satisfy the valence requirements of the carbon atoms when one hydrogen atom is attached to each carbon atom. Since the properties of benzene are not similar to those of an unsaturated compound, it has been assumed that the double bonds between the carbon atoms in a ring are not as easily broken as those in an open chain compound.

For ease of representation, benzene is often indicated as a hexagon, with or without the double bonds:



Benzene
 C_6H_6



Benzene
 C_6H_6



Phenyl Radical
 C_6H_5

In using these symbols, it must be kept in mind that alternate double bonds are present, and that a hydrogen atom is attached to each carbon atom. If an element or radical has replaced a hydrogen atom on the ring, this must be indicated.

Benzene is a colorless liquid, insoluble in water, but soluble

CHAPTER XII

Cyclic Compounds

ORIGINALLY all carbon compounds were divided into *aliphatic* and *aromatic* compounds, much as chemistry was divided into *organic* and *inorganic*. The word aromatic was chosen because many of the naturally occurring derivatives of benzene such as oil of wintergreen, vanillin, oil of bitter almonds, and turpentine oil had an agreeable aroma and were therefore put in a class by themselves. However, a classification based on aroma alone is of little value, since many aliphatic compounds have pleasant odors and many that belong to the aromatic series have no odor.

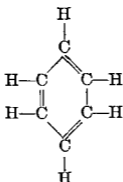
At present we divide organic compounds into the *aliphatic* and the *cyclic*, or *ring*, compounds. Aliphatic compounds are composed of open chains of carbon atoms, while the cyclic compounds have their carbon atoms in a closed chain or ring structure. When the closed chain is made up entirely of carbon atoms, the compounds are called *carbocyclic*; when other kinds of atoms besides carbon are also present in the ring, they are called *heterocyclic* compounds. The name aromatic has been retained and is applied to compounds that are derivatives of the carbocyclic hydrocarbon, benzene.

AROMATIC COMPOUNDS

Benzene

Since benzene is the basic substance from which aromatic compounds are derived, it is the most important cyclic compound. Benzene is a hydrocarbon having the empirical formula C_6H_6 . If benzene were written as an open chain structure, it would be a highly unsaturated hydrocarbon. Its chemical prop-

erties, however, more closely resemble those of a saturated hydrocarbon. For many years chemists were unable to decide on a structural formula that would account for the reactions and properties of benzene. In 1865, Kekule proposed a ring structure for benzene which is generally accepted today. The structural formula for benzene was represented as 6 carbons combined in the form of a hexagon with alternate single and double bonds:



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 C_6H_6



Benzene
 C_6H_6



Phenyl Radical
 C_6H_5

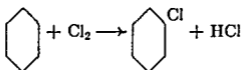
In using these symbols, it must be kept in mind that alternate double bonds are present, and that a hydrogen atom is attached to each carbon atom. If an element or radical has replaced a hydrogen atom on the ring, this must be indicated.

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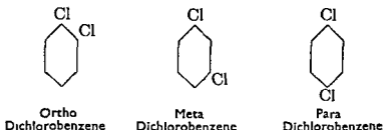
in alcohol and ether. It is used as a solvent for fats, resins, varnishes, and rubber. Commercially it is used as the starting material in the manufacture of many important aromatic compounds. Sometimes benzene is mixed with gasoline and used as a fuel in internal combustion engines. It is toxic when taken internally. Prolonged inhalation of its vapors by industrial workers results in a decreased production of red and white corpuscles in the blood, which may prove fatal.

Halogen Derivatives of Benzene

Halogens such as chlorine and bromine react with benzene to form substitution products in which one or more of the hydrogen atoms are replaced by an atom of the halogen:



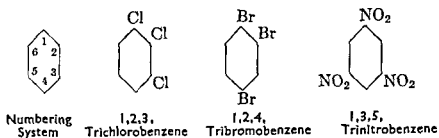
When two or more halogen atoms are substituted on the benzene ring, their relative position is important. For example, there are three dichlorobenzenes which may be represented as follows:



The isomer in which the two chlorine atoms are on adjacent carbon atoms is called *ortho*, abbreviated *o*-. When there is one carbon atom between the two substituted groups, the isomer is known as *meta* (*m*-), while the isomer in which there are two carbon atoms between the two chlorine atoms is termed *para* (*p*-).

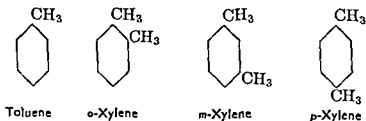
Any two groups that are substituted for hydrogen on the benzene ring will be in the *ortho*, *meta*, or *para* position. When

three or more groups are substituted for the hydrogen in benzene. their positions are indicated by numbers:



Homologues of Benzene

Any radical or group of elements attached to the benzene ring is known as a side chain. There are higher members or *homologues* in the benzene series that differ from each other by 1 carbon and 2 hydrogen atoms (CH_2 ; as did the homologues of the methane series). The first higher homologue is *toluene*, $\text{C}_6\text{H}_5\text{CH}_3$, which is obtained from the light oil distilled from coal tar. Toluene is a colorless liquid which is insoluble in water and has a characteristic odor. It is used as a preservative for urine specimens and for the preparation of many more complicated aromatic compounds. Large quantities of toluene are used in the manufacture of the explosive, trinitrotoluene, commonly called T. N. T. The second higher homologue of benzene is known as *xylene*. Since xylene contains two methyl groups, it may exist as the ortho, meta, or para isomer. Toluene and the isomers of xylene may be written structurally as follows:



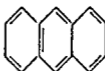
The xylenes, obtained from the light oil distilled from coal tar, have properties similar to toluene.

Condensed Aromatic Compounds

Two or more benzene rings may combine to form aromatic compounds with condensed or fused benzene rings. The simplest compound of this type is *naphthalene*. It consists of two rings fused together so that two carbon atoms are common to each ring.



Naphthalene



Anthracene

Naphthalene and anthracene are obtained from coal tar and are used industrially in the manufacture of dyes and dye intermediates. Large quantities of the white crystalline solid, naphthalene, are used in the preparation of moth balls.

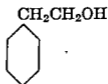
Oxygen Derivatives

Aromatic hydrocarbons have oxygen derivatives that correspond to the aliphatic oxygen compounds. Therefore, we have aromatic alcohols, aldehydes, ketones, and acids that contain the same characteristic groups we encountered in the aliphatic series. When a characteristic group or radical is in a side chain attached to the benzene ring, the compound reacts in a similar fashion to the corresponding aliphatic compound.

Aromatic alcohols have the OH group in the side chain. Benzyl alcohol and phenyl ethyl alcohol are the two lowest members in the series:



Benzyl Alcohol



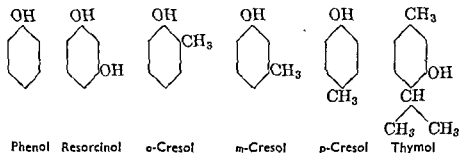
Phenyl Ethyl Alcohol

Both of these compounds possess pleasant odors and are used in the manufacture of perfumes. Aromatic alcohols react like aliphatic alcohols. When benzyl alcohol is oxidized, the first prod-

uct is benzaldehyde; further oxidation results in the formation of benzoic acid.

Phenols

When the OH group is attached directly to the benzene ring, the aromatic derivatives are known as *phenols*. The hydroxy group in phenols is much more acidic than the OH group in aliphatic alcohols. The acidic nature of the phenols is illustrated by their ability to turn blue litmus paper red and to react with inorganic bases to form a salt. The simplest member of this series, known as *phenol*, or *carbolic acid*, is shown below with other typical phenols:



Phenols are colorless liquids or solids that are soluble in alcohol and ether and usually have a characteristic odor.

Phenol, or carbolic acid, has strong antiseptic properties but is a poison when taken internally. Since it blisters the skin, it should be washed off immediately with alcohol or ether. A dilute solution (3 per cent) of phenol is an effective disinfectant for surgical instruments and containers used in the hospital. Large quantities of phenol are used in the manufacture of drugs, dyes, explosives, and plastics.

The *cresols* can be considered as methyl derivatives of phenol or hydroxy derivatives of toluene. They are stronger disinfectants than the phenols and are less toxic. *Lysol* is a disinfectant composed of a mixture of cresols in a soap solution. Thymol, obtained from the oils of thyme and mint, is a cresol derivative with a pleasant odor. It is an effective antiseptic used in mouthwashes, toothpastes, and in the treatment of hookworm.

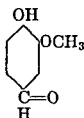
Picric acid, 2, 4, 6-trinitrophenol, is formed by heating phenol with nitric acid. The bright yellow solid is used with other dyes to color wool and silk. It is commonly employed in the treatment of burns, since it forms insoluble compounds with the protein of the skin and damaged tissue, covering the burn with a protective coating. *Butesin picrate* is a salve that combines picric acid with a local anesthetic to relieve the pain of burns.

Aromatic Aldehydes

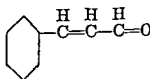
The aromatic aldehydes contain the aldehyde group -CHO attached to one of the carbons in the benzene ring or attached to a carbon in a side chain. The simplest aromatic aldehyde, *benzaldehyde*, occurs in the oil of bitter almonds.



Benzaldehyde



Vanillin

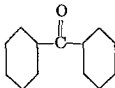


Cinnamic Aldehyde

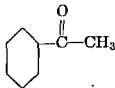
Vanillin, an aromatic aldehyde found in vanilla beans, is responsible for the taste of vanilla extract. *Cinnamic aldehyde* is an unsaturated aldehyde which occurs in oil of cinnamon. All three of these aldehydes are used in flavorings.

Aromatic Ketones

The characteristic ketone group —CO— is present in aromatic ketones where it may be attached to two aromatic rings or to an aromatic and an aliphatic group. An example of the former class would be *benzophenone*, while the latter type could be represented by *acetophenone*:



Benzophenone



Acetophenone

Acetophenone, a colorless oil with a characteristic odor, is used as a hypnotic. If one of the hydrogens on the carbon atom at the end of the side chain is replaced by a chlorine atom, the compound *chloroacetophenone* is formed. This compound is commonly used as tear gas.

Aromatic Acids

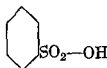
Aromatic acids contain the carboxyl group—COOH attached to a carbon in the benzene ring or in a side chain. *Benzoic acid*, the simplest aromatic acid, has one carboxyl group attached directly to the benzene ring. Another important acid is *salicylic acid*, which is a hydroxy aromatic acid. *Benzene sulfonic acid* is a substituted aromatic acid that is formed by the reaction of sulfuric acid and benzene.



Benzoic Acid



Salicylic Acid

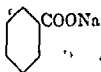


Benzene Sulfonic Acid

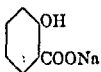
Benzoic and salicylic acids form salts and esters that are more important than the free acids. Derivatives of benzene sulfonic acid find frequent use in medical practice. *Saccharin* is derived from *o*-sulfobenzoic acid and is used as a sweetening agent in cases where the sugar intake must be restricted. *Chloramine T*, a sulfonic acid derivative of toluene, is a surgical antiseptic. *Phenolsulfonephthalein* (phenol red) is a derivative of sulfobenzoic acid and phenol; it is used as a pH indicator and as a dye in kidney function tests

Aromatic Salts and Esters

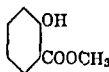
Benzoic acid and salicylic acid readily form salts and esters that are important analgesics and antiseptics. Upon treatment with sodium hydroxide, the sodium salt of these acids is formed. Salicylic acid reacts with methyl alcohol and with acetic acid to form esters.



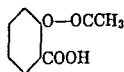
Sodium Benzoate



Sodium Salicylate



Methyl Salicylate

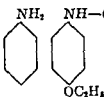


Acetylsalicylic Acid

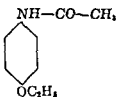
The antiseptic properties of *sodium benzoate* and *sodium salicylate* are made use of in food preservatives. They are also effective analgesics in the treatment of rheumatism and arthritis. *Methyl salicylate* has the odor of wintergreen and is used as a flavoring agent. Because it has the ability to penetrate the skin, it is used as an analgesic in liniments and salves. *Acetylsalicylic acid*, or *aspirin*, is a common drug used by millions of people. Over 5000 tons of *aspirin* are produced in the United States every year.

Aromatic Amines

Aromatic compounds that contain the amino group —NH_2 are known as *aromatic amines*. As in the case of aliphatic amines, there are primary, secondary, and tertiary aromatic amines. The simplest primary aromatic amine, aminobenzene, is commonly called *aniline*. Aniline is a reactive substance which forms many derivatives that possess medicinal properties.



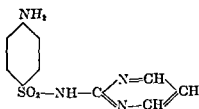
Aniline



Phenacetin



Sulfanilamide



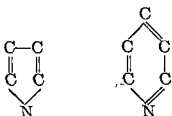
Sulfadiazine

Phenacetin is used to reduce fevers and is the active component in many remedies for headache and neuralgia. *Sulfanilamide* has been widely used since 1936 in the treatment of cases of streptococcus infections, pneumonia, puerperal fever, gonorrhea, and gas gangrene. Since the administration of this drug often causes toxic reactions, many other similar derivatives have been prepared and tested. Sulfapyridine, sulfathiazole, sulfaguanidine, and sulfadiazine are among these derivatives. The last named

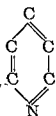
drug is less toxic than the others, yet is one of the most effective in the treatment of pneumonia and staphylococcus infections.

HETEROCYCLIC COMPOUNDS

As stated previously, heterocyclic compounds contain atoms other than carbon, such as nitrogen, oxygen, and sulfur in the ring structure. Heterocyclic compounds may have a nucleus of a five- or six-membered ring, or may be a combination of benzene with one of these rings. Some typical heterocyclic nuclei are shown as follows:



Pyrrole Nucleus



Pyridine Nucleus



Indole Nucleus



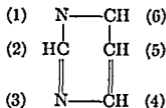
Quinoline

Pyrrole is a constituent of *hemoglobin*, the respiratory pigment of the blood, and of *chlorophyll*, the plant pigment. It is present in certain drugs and in two of the amino acids that make up the protein molecule. *Pyridine* is a component of *nicotinic acid*, which is one of the vitamins in the vitamin B complex. *Nicotinic acid*, renamed "niacin," is essential for the prevention of the dietary disease, pellagra. At present it is used along with other vitamins in the fortification of flour and cereals. *Sulfapyridine* is one of the sulfa drugs used in the treatment of streptococcus infections. The *indole* nucleus is present in the amino acid *tryptophan*, and in the products of protein putrefaction known as *indole* and *skatole*.

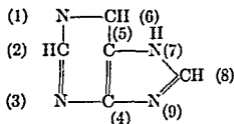
Quinoline is a constituent of *quinine*, *cinchonine*, and other alkaloids. It is an effective antiseptic and is a component of many medical preparations.

Pyrimidines and Purines

The heterocyclic compounds known as *pyrimidines* and *purines* are derivatives of the following nuclei:



Pyrimidine



Purine

Pyrimidine is the cyclic structure present in barbituric acid, which is the parent substance of the hypnotic drugs called *barbiturates*. Two of the members of the vitamin B complex, *thiamine* and *riboflavin*, contain a pyrimidine nucleus in their structure. Both pyrimidines and purines are essential constituents of the nucleic acids present in the nuclear tissue of plants and animals. When nucleic acids combine with proteins, the resulting compound is called a *nucleoprotein*. Common pyrimidines such as uracil and cytosine, and purines such as adenine and guanine, are present in nucleic acids. When nucleic acids are oxidized in the body, they yield *uric acid* (2, 6, 8-trioxy purine) as the end product. Uric acid normally is excreted in the urine. In abnormal conditions, it may form insoluble deposits in the joints (in gout) or in the kidney as kidney stones. The stimulants *caffeine* in tea and coffee and *theobromine* in cocoa are methylated purines.

Alkaloids

Alkaloids are basic nitrogen-containing substances that occur in plants. They generally have a heterocyclic ring in their structure and are characterized by marked physiological activity. Most of the alkaloids are white crystalline solids with a bitter taste.

Alkaloids are grouped according to the heterocyclic nucleus they contain. Typical alkaloids that contain the *pyridine nucleus* are *coniine*, *nicotine*, and *arecoline*. Coniine is the active principle of the poison hemlock plant. Nicotine is the alkaloid obtained from the tobacco plant. Large quantities of nicotine are used in the preparation of insecticides and plant sprays. It is also used

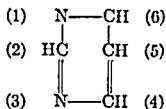
to destroy lice on poultry. Arecoline is the principal alkaloid of the fruit of the betel nut palm. Betel chewing results in a mild stimulation and a craving for the drug.

Cocaine and *atropine* are the most important members of the group of alkaloids which are derivatives of the heterocyclic nucleus *tropane*. Cocaine, obtained from the leaves of the coca plant, was formerly used as a local anesthetic in dentistry and eye surgery. The drug is somewhat toxic; its continued use is habit-forming, and eventually produces mental deterioration. A substitute, known as *procaine*, or *novocaine*, was developed to overcome the disadvantages of cocaine. Atropine is present in the root of the deadly nightshade, or belladonna plant. This alkaloid is commonly used to dilate the pupil of the eye to facilitate examination of its interior.

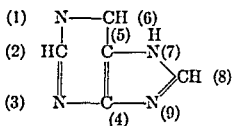
The group of alkaloids that contain the *quinoline* nucleus include *quinine*, *morphine*, *codeine* and *strychnine*. Quinine, obtained from the bark of the cinchona tree, is used in the treatment of malaria and to reduce fevers. It is able to poison the parasite that causes malaria without harming the host. Morphine is the alkaloid in opium that is mainly responsible for its physiological activity. It acts by depressing the central nervous system. In small doses it relieves pain, while larger doses produce sleep. Codeine has a structure similar to morphine and is also obtained from the opium poppy. It is less toxic than morphine and is effective in relieving pain. Both morphine and codeine are habit-forming narcotics. Strychnine is found in the seeds of the *nux vomica* plant. In very small doses, strychnine has a stimulating effect and is used in tonics such as I. Q. and S., which contains iron, quinine, and strychnine. In large amounts, it is very poisonous and causes muscular convulsions.

REVIEW QUESTIONS

1. Why were cyclic compounds originally termed "aromatic"?
2. Write the complete structural formula for benzene. How do we usually represent a molecule of benzene in writing organic reactions?
3. Differentiate between ortho, meta, and para derivatives of organic compounds



Pyrimidine



Purine

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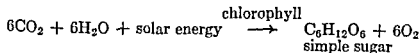
CHAPTER XIII

Carbohydrates

FROM the standpoint of biochemistry, the three most important classes of organic compounds are the carbohydrates, lipids, and proteins. These substances make up the major portion of all foods and plant and animal tissues. The carbohydrates have the simplest chemical structure and are therefore considered first. As a class of compounds, they include starches and celluloses which are widely distributed in nature. Simple sugars such as glucose, fructose, and sucrose are found in many fruits and vegetables. Starches are the storage form of carbohydrates in plants, while the woody structure of trees and plants is mainly cellulose.

SYNTHESIS

Carbohydrates are formed in the cells of plants from carbon dioxide and water. In the presence of sunlight and chlorophyll, the green pigment of leaves, these two compounds react to form simple sugars:



This important process by which plants form food material by means of the energy of sunlight is called *photosynthesis*. Although photosynthesis is represented as a simple chemical reaction, it involves complex mechanisms that are not as yet completely understood. Since radioactive elements have become available, the reactions of photosynthesis are being studied with the help of radioactive carbon.

4. Write the formula for 1,3,6-trihydroxy benzene; 1-chloro-4,6-dinitrobenzene; and 1,2,3-tribromo-5-hydroxybenzene.
5. What is a homologue? Name and write the formulas of two homologues of benzene.
6. Write the formulas for three different phenols. What properties of phenol, cresols, and picric acid are applied in nursing practice?
7. Write the formulas for an aromatic alcohol, aldehyde, ketone, acid, and salt. Name each compound.
8. In what class of aromatic compounds does aspirin belong? What is the chemical name for this compound? Write the formula for aspirin.
9. What recently developed antibacterial agents are derivatives of aromatic amines?
10. What are heterocyclic compounds? Name several heterocyclic compounds that are used in medicine.
11. Name three therapeutic agents that contain the pyrimidine nucleus.
12. List several alkaloids that are used in medicine, and the heterocyclic nucleus they contain.

CLASSIFICATION

The simplest carbohydrates are known as *monosaccharides*, or *simple sugars*. Monosaccharides are straight chain polyhydric alcohols and are classified according to the number of carbon atoms in the chain. A sugar with 2 carbon atoms is called a diose, with 3 a triose, with 4 a tetrose, with 5 a pentose, and with 6 a hexose. The ending *-ose* is characteristic of sugars. When two monosaccharides are linked together by splitting out a molecule of water, the resulting compound is called a *disaccharide*. The combination of three monosaccharides results in a *trisaccharide*, while a compound sugar composed of several monosaccharides is called a *polysaccharide*.

Physiologically important carbohydrates may be classified as follows:

I. Monosaccharides

Pentose— $C_5H_{10}O_5$:

Aldoses—Arabinose

Xylose

Ribose

Hexoses— $C_6H_{12}O_6$:

Aldoses—Glucose

Galactose

Ketoses—Fructose

II. Disaccharides— $C_{12}H_{22}O_{11}$

Sucrose (glucose + fructose)

Maltose (glucose + glucose)

Lactose (glucose + galactose)

III. Polysaccharides

Hexosans.

Glucosans—Starch

Glycogen

Dextrin

Cellulose

Trioses

A triose is the simplest monosaccharide that can exist as an aldose or a ketose. Trioses are derivatives of the polyhydric alcohol, glycerol:

Animals lack the ability to synthesize carbohydrates from inorganic materials and must obtain their supply of carbohydrates by eating plants. When animals take in carbohydrates in their diet, the oxygen from respiration oxidizes the sugar to carbon dioxide and water with the liberation of energy which is used by the body:



The above reactions represent a cycle in which plants and animals are the participants. In the process of photosynthesis, plants liberate oxygen, which is essential to animal life. During respiration animals give off carbon dioxide, which is used by the plant to synthesize carbohydrates and other food materials. It has been stated that there is no reaction known to man which is of greater importance than that of photosynthesis. This is one of the few reactions that convert the energy of the sun into the chemical energy of foods. It is estimated that about 1 per cent of the energy of the sunshine falling on the plant is converted into energy, which is then stored in the form of carbohydrates.

COMPOSITION

Carbohydrates are composed of carbon, hydrogen, and oxygen, and the hydrogen and oxygen are usually in the proportion of two to one, the same as in water. The name carbohydrate (which signifies hydrate of carbon) is based on this relationship of hydrogen and oxygen. The term is misleading, however, because water does not exist as such in a carbohydrate. The classical definition of a carbohydrate stated that they were compounds of C, H, and O in which the H and O were in the same proportion as in water. However, certain compounds such as acetic acid, $\text{C}_2\text{H}_4\text{O}_2$, and lactic acid, $\text{C}_3\text{H}_6\text{O}_3$, fit this definition but are not classed as carbohydrates, while a carbohydrate such as rhamnose, $\text{C}_6\text{H}_{12}\text{O}_5$, does not fit the definition. Carbohydrates are now defined as derivatives of polyhydric alcohols containing an aldehyde or ketone group. A sugar that contains an aldehyde group is called an *aldose*, one that contains a ketone group is termed a *ketose*.

CLASSIFICATION

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Aldoses—Arabinose

Xylose

Ribose

Hexoses— $C_6H_{12}O_6$:

Aldoses—Glucose

Galactose

Ketoses—Fructose

II. Disaccharides— $C_{12}H_{22}O_{11}$

Sucrose (glucose + fructose)

Maltose (glucose + glucose)

Lactose (glucose + galactose)

III. Polysaccharides

Hexosans:

Glucosans—Starch

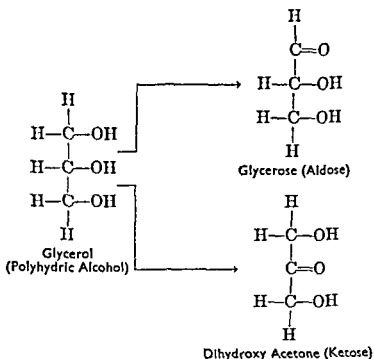
Glycogen

Dextrin

Cellulose

Trioses

A triose is the simplest monosaccharide that can exist as an aldose or a ketose. Trioses are derivatives of the polyhydric alcohol, glycerol:



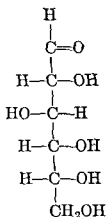
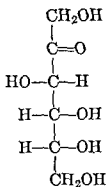
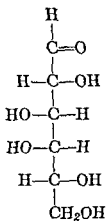
Pentoses

The pentoses are sugars whose molecules contain 5 carbon atoms. They most commonly occur in nature, combined in polysaccharides, from which the monosaccharides may be obtained by hydrolysis with acids. Arabinose is obtained from gum arabic and the gum of the cherry tree. Xylose is found in wood, straw, and corn cobs. Ribose is a constituent of a nucleic acid found in plants.

Hexoses

The most important monosaccharides from a biochemical standpoint are the hexoses. Three of these are nutritionally important. Two belong to the aldose group and are glucose and galactose. The third belongs to the ketose group and is called fructose.

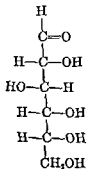
Although all hexoses have the same empirical formula, $\text{C}_6\text{H}_{12}\text{O}_6$, each has a different molecular arrangement as illustrated in the structural formulas for glucose, fructose, and galactose.

Glucose
(Aldose)Fructose
(Ketose)Galactose
(Aldose)

REACTIONS OF CARBOHYDRATES

Reducing Power

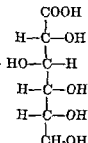
Since aldehyde and ketone groups are reducing groups, sugars that contain these in a free form exhibit reducing powers. This reducing property can be utilized to test for the presence of these sugars in blood or urine. *Benedict's solution* is widely used in testing urine for glucose and may be considered as a solution of blue cupric hydroxide, $\text{Cu}(\text{OH})_2$. When a sugar solution containing a free aldehyde or ketone group is heated with Benedict's solution, the $\text{Cu}(\text{OH})_2$ is reduced to form an orange precipitate of Cu_2O . When only a small amount of sugar is present, the slight precipitate often appears green when its orange color is mixed with the blue color of Benedict's solution. The aldehyde or ketone groups of the sugar take up the oxygen that is released from the $\text{Cu}(\text{OH})_2$ and are oxidized to form carboxyl groups.



Glucose

+ $2\text{Cu}(\text{OH})_2$
Cupric Hydroxide
in
Benedict's Solution

$\longrightarrow \text{Cu}_2\text{O} \downarrow + 2\text{H}_2\text{O} +$
Cuprous Oxide
an
Orange Precipitate

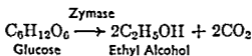


Gluconic Acid

Other metallic hydroxides such as AgOH and Bi(OH)_2 are reduced by sugars to form metallic silver and bismuth respectively; these are also used to test for the presence of sugars.

Fermentation

The enzyme *zymase* present in common bread yeast will act on some of the hexose sugars to produce alcohol and carbon dioxide. The fermentation of glucose may be represented as follows:



The common hexoses (with the exception of galactose) ferment readily, but pentoses are not fermented by yeast. Disaccharides must first be converted into their monosaccharide constituents by other enzymes present in yeast before they are susceptible to fermentation by zymase.

There are many other types of fermentation of carbohydrates besides the common alcoholic fermentation. When milk sours, the lactose of milk is converted into lactic acid by a fermentation process. Citric acid, acetic acid, butyric acid, and oxalic acid may all be produced by special fermentation processes.

Oxidation of Carbohydrates

The alcohol, aldehyde, and ketone groups of sugars may be oxidized to produce a variety of oxidation products. When the primary alcohol group on the end of the carbon chain of glucose is oxidized to a carboxyl group, *glucuronic acid* is formed. This compound is the most important oxidation product of glucose; it unites with toxic substances in the body, forming nontoxic compounds which are eliminated in the urine. If the aldehyde group of glucose is oxidized, the product is called *gluconic acid*, while the oxidation of both the primary alcohol and the aldehyde group produces a compound called *saccharic acid*. Other sugars oxidize in a manner similar to that of glucose.

Reduction of Carbohydrates

Simple sugars may be reduced to form the polyhydric alcohols from which they are derived. On reduction, glucose yields *sorbitol*, fructose gives both *sorbitol* and *mannitol*, and galactose forms *dulcitol*. Of these polyhydric alcohols, *sorbitol* is the most important because it is used in the manufacture of synthetic vitamin C.

MONOSACCHARIDES

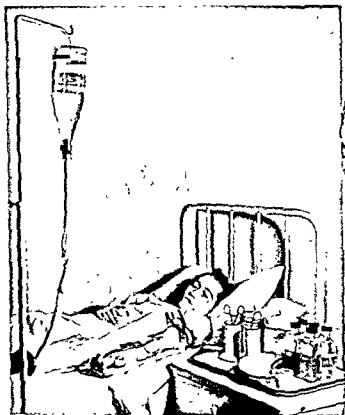


Fig. 35. An apparatus for the continuous intravenous administration of glucose. (From Goodnow, M.: *The Technic of Nursing*. Philadelphia, W. B. Saunders Company.)

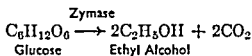
Glucose

Glucose is also called *dextrose*, or grape sugar, and occurs with fructose in many sweet fruits. It ranks third in sweetness, being surpassed only by fructose and sucrose. It is the most

Other metallic hydroxides such as AgOH and Bi(OH)_2 are reduced by sugars to form metallic silver and bismuth respectively; these are also used to test for the presence of sugars.

Fermentation

The enzyme *zymase* present in common bread yeast will act on some of the hexose sugars to produce alcohol and carbon dioxide. The fermentation of glucose may be represented as follows:



The common hexoses (with the exception of galactose) ferment readily, but pentoses are not fermented by yeast. Disaccharides must first be converted into their monosaccharide constituents by other enzymes present in yeast before they are susceptible to fermentation by *zymase*.

There are many other types of fermentation of carbohydrates besides the common alcoholic fermentation. When milk sours, the lactose of milk is converted into lactic acid by a fermentation process. Citric acid, acetic acid, butyric acid, and oxalic acid may all be produced by special fermentation processes.

Oxidation of Carbohydrates

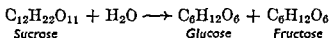
The alcohol, aldehyde, and ketone groups of sugars may be oxidized to produce a variety of oxidation products. When the primary alcohol group on the end of the carbon chain of glucose is oxidized to a carboxyl group, *glucuronic acid* is formed. This compound is the most important oxidation product of glucose; it unites with toxic substances in the body, forming nontoxic compounds which are eliminated in the urine. If the aldehyde group of glucose is oxidized, the product is called *gluconic acid*, while the oxidation of both the primary alcohol and the aldehyde group produces a compound called *saccharic acid*. Other sugars oxidize in a manner similar to that of glucose.

reduce Benedict's solution. One such as maltose, however, in which the linkage connects the aldehyde group of one monosaccharide with a hydroxyl group of the other, will readily reduce Benedict's solution. In general, disaccharides such as maltose and lactose that reduce Benedict's solution possess properties similar to those of the monosaccharides.

Sucrose

Sucrose is commonly called *cane sugar* and is the ordinary sugar that is used for sweetening purposes in the home. It is found in many plants like sugar cane, sugar beets, sorghum cane, and in the sap of the sugar maple. Commercially it is prepared from sugar cane and sugar beets.

Sucrose is composed of a molecule of glucose joined to a molecule of fructose in such a way that the linkage involves the reducing groups of both sugars. It is the only common mono- or disaccharide that will not reduce Benedict's solution. When sucrose is hydrolyzed, either by the enzyme sucrase or by an acid, a molecule of glucose and a molecule of fructose are formed.



The fermentation of sucrose by yeast is possible since the yeast contains both enzymes, sucrase and zymase. The sucrase first hydrolyzes the sugar and then the zymase ferments the monosaccharides to form alcohol and carbon dioxide.

Lactose

The disaccharide present in milk is lactose, or *milk sugar*. It is synthesized in the mammary glands of animals from the glucose in the blood. Commercially it is obtained from milk whey and is used in infant foods and special diets. Lactose, when hydrolyzed by the enzyme lactase or by an acid, forms a molecule of glucose and a molecule of galactose. Lactose will reduce Benedict's solution, but is not fermented by yeast. Certain bacteria contain enzymes that will ferment lactose to form lactic acid. This process occurs when milk sours. It has been suggested

important sugar from a physiological standpoint, as it is the normal sugar of the blood and tissue fluids. In diabetes mellitus, the amount of glucose in the blood increases and it often appears in the urine. In the United States, considerable quantities of glucose are made commercially by the acid hydrolysis of corn-starch. Corn syrup is prepared by the same process; it contains maltose and dextrins in addition to glucose. Many formulas for modifying cow's milk in infant feeding include corn syrup as a source of carbohydrates. Since glucose is the normal blood sugar, it is often given to patients intravenously (Fig. 35), when they are unable to take food by mouth.

Fructose

Fructose is often called *fruit sugar*, or *levulose*, and is the only important ketose sugar. It occurs with glucose in fruits and honey. It is the sweetest sugar known, having twice the sweetness of glucose and five times that of galactose. Fructose, usually prepared by the acid hydrolysis of the polysaccharide, inulin, is a constituent of the disaccharide sucrose, or cane sugar.

Galactose

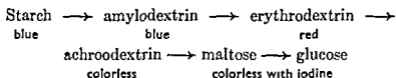
This sugar is not formed free in nature but occurs as a constituent of the disaccharide lactose. *Agar-agar* is a polysaccharide of galactose that is used as a culture medium in bacteriology. Brain and nervous tissue in the animal body contain galactose as an essential constituent.

DISACCHARIDES

The disaccharides are sugars that are composed of two monosaccharides linked together through the loss of a molecule of water. The linkage is always made from the aldehyde group of one of the sugars to a hydroxyl or ketone group of the second. In order to reduce Benedict's solution, disaccharides must have an aldehyde or ketone group that is not involved in the linkage between the two sugars. A disaccharide such as sucrose in which the two monosaccharides are joined by a link between the aldehyde group of glucose and the ketone group of fructose will not

glucose molecules. In plant cells, it exists as small granules, the shape of which is characteristic of the plant. The granules are covered by a layer of *amylopectin* which must be ruptured before the starch will mix with water to form a colloidal solution. Cooking destroys this outer layer, making the starch more readily digestible. Starch will not reduce Benedict's solution and is not fermented by yeast.

When starch is hydrolyzed by enzymes or by an acid, it is split into a series of intermediate compounds possessing smaller numbers of glucose units. The product of complete hydrolysis is the free glucose molecule. A characteristic reaction of starch is the formation of a blue compound with iodine. This test is often used to follow the hydrolysis of starch, since the color changes from blue through red to colorless with decreasing molecular weight:



Dextrin

Dextrins are found in germinating grains but are usually obtained by the partial hydrolysis of starch. They are soluble in water and have a slightly sweet taste. Large quantities of dextrins are used in the manufacture of adhesives because they form sticky solutions when wet. An example of their use is the mucilage on the back of postage stamps.

Glycogen

Glycogen is the storage form of carbohydrate in the animal body and is often called animal starch. It is found in liver and muscle tissue. It is soluble in water, does not reduce Benedict's solution, and gives a wine-red color with iodine. The glycogen molecule is similar to starch and is thought to contain about 12 glucose molecules, whereas starch contains about 24 to 30 glucose units. When glycogen is hydrolyzed in the animal body, it forms glucose to help maintain the normal sugar content of the blood.

that one of the purposes of lactose in milk is to furnish galactose for the formation of brain and nervous tissue in infants.

Maltose

Maltose is present in germinating grains. Since it is obtained as a product of the hydrolysis of starch by enzymes present in malt, it is often called *malt sugar*. It is also formed in the animal body by the action of enzymes on starch in the process of digestion. Commercially it is made by the partial hydrolysis of starch by acid in the manufacture of corn syrup. Maltose reduces Benedict's solution and is fermented by yeast. On hydrolysis it forms two molecules of glucose.

POLYSACCHARIDES

The polysaccharides are complex carbohydrates that are made up of many monosaccharide molecules and therefore possess a high molecular weight. They differ from the simple sugars in many ways. They fail to reduce Benedict's solution, do not have a sweet taste, and are usually insoluble in water. When dissolved by chemical means, they form colloidal solutions because of their large molecules.

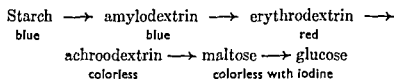
There are polysaccharides formed from pentoses or from hexoses, and the so-called mixed polysaccharides. Of these the most important are composed of the hexose glucose and are called *hexosans*. As in a disaccharide, whenever two molecules of a hexose combine, a molecule of water is split out. For this reason, a hexose polysaccharide may be represented by the formula $(C_6H_{10}O_5)_x$. The x represents the number of hexose molecules in the individual polysaccharide. Because of the complexity of the molecules, the number of glucose units in any one polysaccharide is still an estimate.

Starch

From a nutritional standpoint, starch is the most important polysaccharide. It is made up of glucose units and is therefore the storage form of carbohydrates in plants. It has been estimated that a starch molecule is composed of about 24 to 30

glucose molecules. In plant cells, it exists as small granules, the shape of which is characteristic of the plant. The granules are covered by a layer of *amylopectin* which must be ruptured before the starch will mix with water to form a colloidal solution. Cooking destroys this outer layer, making the starch more readily digestible. Starch will not reduce Benedict's solution and is not fermented by yeast.

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Cellulose

Cellulose is a polysaccharide found in the framework or supporting structure of plants. It is made up of glucose units but is not hydrolyzed by any of the enzymes in the human digestive tract and therefore cannot be used as a source of dietary carbohydrates. Cellulose will not reduce Benedict's solution and is insoluble in water.

The chemical treatment of cellulose has resulted in several important commercial products. When treated with nitric acid, cellulose is converted into nitrocelluloses. A common nitrocellulose, guncotton, is used in the manufacture of high explosives. Another is pyroxylin, used as a waterproof coating for book bindings, upholstery, and luggage. Pyroxylin may be dissolved in organic solvents to form such materials as collodion, celluloid, and lacquers. Cellulose treated with acetic acid forms cellulose acetate, which is used in x-ray and motion picture films and in textile fibers. Rayon is produced by treating cellulose with sodium hydroxide and carbon disulfide. The solution that results from this treatment is forced through fine holes into dilute sulfuric acid to make the rayon fibers. Rayon fabrics are finding increased usage at the present time as a substitute for silk. Cellophane is made by a process similar to that used for rayon.

SUMMARY

The characteristic properties and the end products of hydrolysis of the important carbohydrates discussed in this chapter are outlined in the table on the following page. You will observe that dextrin is listed as giving a slight reduction of Benedict's solution. In general, polysaccharides do not reduce Benedict's solution; however, the dextrans are partial hydrolysis products of starch and often contain small amounts of maltose or glucose which are responsible for the positive Benedict's test.

Carbohydrate	Reduction of Benedict's Solution	Fermentation with Yeast	Color with Iodine	End Product of Hydrolysis
Glucose	+	+	-	-
Fructose	+	+	-	-
Galactose	+	-	-	-
Sucrose	-	+	-	glucose and fructose
Lactose	+	-	-	glucose and galactose
Maltose	+	+	-	glucose and glucose
Starch	-	-	blue	glucose
Dextrin	+(slight)	-	purple	glucose
Glycogen	-	-	red	glucose
Cellulose	-	-	-	glucose

REVIEW QUESTIONS

1. Chlorophyll is necessary in photosynthesis for the production of sugar from carbon dioxide and water. What role would you assume chlorophyll to play in this reaction? Why?
2. How does photosynthesis in plants and oxidation in animals fit into a cycle that is beneficial to both plants and animals?
3. Give the classical and modern definition of carbohydrates. Which is the more accurate? Explain.
4. Define the following terms: aldose, ketose, disaccharide, polysaccharide, pentose, and hexose. Give an example of each.
5. Glucose, fructose, and galactose are all

6. What two fundamental reactions occur in the Benedict's test? Which is the more important with respect to the interpretation of the test?
7. Name two types of fermentation. What products are formed in the fermentation of sugars by zymase in yeast?
8. Name an important oxidation product of glucose, and a compound formed by reduction. Of what importance is each of these compounds?
9. Give three names for glucose. Why is this sugar so important from a physiological standpoint?
10. Explain why a disaccharide like sucrose fails to reduce Benedict's reagent whereas one like maltose will reduce it.
11. What agents may be used to hydrolyze the three important disaccharides? What products would result from the hydrolysis of sucrose, lactose, and maltose?
12. Is sucrose fermented by yeast? Explain the process.
13. Why is lactose nutritionally important to infants?
14. In what ways do polysaccharides differ from the simple sugars?
15. How would you describe chemically a polysaccharide composed of pentose units?
16. What are the steps in the process of gradual hydrolysis of starch to form glucose? What simple test may be used to detect the presence of intermediate products during the hydrolysis of starch?
17. How does the starch molecule compare in size with a molecule of dextrin? With a molecule of glycogen?
18. Name six important products that are made from cellulose.
19. What is the outstanding difference between cellulose and starch?
20. What is rayon? How is it made?

CHAPTER XIV

The Lipids

LIPIDS are widely distributed in nature, occurring in both plant and animal cells. In the animal body, they furnish a concentrated form of fuel for energy, and constitute the main store of reserve food supply. The brain and nervous tissue are richly supplied with certain lipids which are essential constituents of protoplasm. Lipids as a class are insoluble in water but soluble in such fat solvents as ether, chloroform, and carbon tetrachloride. They are made up of carbon, hydrogen, and oxygen and in addition may contain phosphorus and nitrogen.

The important lipids may be classified as follows:

Fats—esters of fatty acids and glycerol.

Waxes—esters of fatty acids with alcohols other than glycerol.

Phospholipids—substituted fats containing phosphoric acid and a nitrogenous base.

Glycolipids—compounds that contain a fatty acid, a carbohydrate, a complex alcohol, and nitrogen.

Sterols—high molecular weight cyclic alcohols.

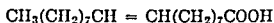
FATTY ACIDS

Since all fats are esters of fatty acids and glycerol, it may be well to consider the composition and properties of these substances before discussing lipids in general. Fatty acids, although not lipids themselves, are found in all of the above types of lipids except the sterols. The fatty acids that occur in nature almost always have an even number of carbon atoms in their molecules. They are usually straight chain organic acids which

may be saturated or unsaturated. Some of the important fatty acids that occur in natural fats are listed in the table below.

In the series of saturated fatty acids, those up to and including capric acid are liquid at room temperature. The most important saturated fatty acids are *palmitic* and *stearic acids*. They are components of the majority of the common animal and vegetable fats.

Unsaturated fatty acids are characteristic constituents of oils. *Oleic acid*, which contains one double bond, is the most common unsaturated fatty acid. Its formula is written:



Name	Formula	Carbon atoms	Occurrence
1. <i>Saturated</i>			
Acetic	CH_3COOH	2	
Butyric	$\text{C}_4\text{H}_7\text{COOH}$	4	Butter fat
Caproic	$\text{C}_6\text{H}_{11}\text{COOH}$	6	Butter fat
Caprylic	$\text{C}_8\text{H}_{15}\text{COOH}$	8	Coconut oil
Capric	$\text{C}_{10}\text{H}_{19}\text{COOH}$	10	Palm kernel oil
Lauric	$\text{C}_{12}\text{H}_{23}\text{COOH}$	12	Coconut oil
Myristic	$\text{C}_{14}\text{H}_{27}\text{COOH}$	14	Nutmeg oil
Palmitic	$\text{C}_{16}\text{H}_{31}\text{COOH}$	16	Animal and vegetable fats
Stearic	$\text{C}_{17}\text{H}_{35}\text{COOH}$	18	Animal and vegetable fats
2. <i>Unsaturated</i>			
Oleic (1=)*	$\text{C}_{17}\text{H}_{33}\text{COOH}$	18	Olive oil
Linoleic (2=)	$\text{C}_{17}\text{H}_{31}\text{COOH}$	18	Linseed oil
Linolenic (3=)	$\text{C}_{17}\text{H}_{29}\text{COOH}$	18	Linseed oil
3. <i>Hydroxy</i>			
Ricinoleic (1=)	$\text{C}_{17}\text{H}_{33}(\text{OH})\text{COOH}$	18	Castor oil
4. <i>Cyclic</i>			
Chaulmoogric	$\text{C}_{17}\text{H}_{31}\text{COOH}$	18	Chaulmoogra oil

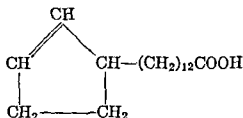
*Number of double bonds.

Ricinoleic acid is an unsaturated fatty acid characterized by the presence of a hydroxyl group and is found in castor oil. Its formula is as follows:



Salts of ricinoleic acid are sometimes used to dextoxify the intestinal contents in cases of colitis.

Chaulmoogric acid is a cyclic fatty acid found in chaulmoogra oil:

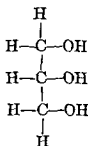


This oil and the ethyl ester of the fatty acid were formerly used as a cure for leprosy, but at present, other therapeutic agents are being used with greater success.

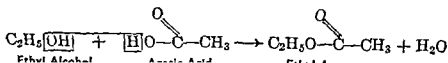
From a nutritional standpoint, the three most commonly occurring fatty acids in edible animal and vegetable fats are palmitic, stearic, and oleic acids.

GLYCEROL

The polyhydric alcohol, *glycerol*, is a common constituent of all fats and oils:



The hydroxyl groups of glycerol will readily form esters with organic acids. The formation of a simple ester may be illustrated by the reaction of the hydroxyl group of ethyl alcohol and the carboxyl group of acetic acid:



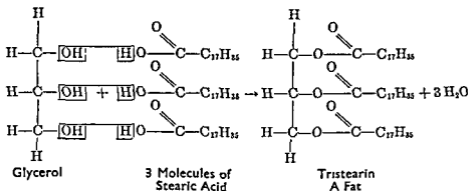
In this equation and in the following one, the fatty acid is written with its carboxyl group turned around facing the hydroxyl group of the alcohol. This is done to bring the two reactive groups close together to better illustrate the splitting out of a molecule of water when the ester linkage is formed.

Since glycerol contains three hydroxyl groups, it will form a triple ester with fatty acids.

FATS

Both fats and oils are esters of fatty acids and glycerol. The main difference between fats and oils is the relatively high content of unsaturated fatty acids in the oils. For this reason, the fats are solid at room temperature, while oils are liquid. A fat that contains short chain fatty acids may also exist as a liquid at room temperature.

The formation of a fat from glycerol and fatty acids may be illustrated as follows:



If all of the fatty acids in a fat are the same (as in tristearin), the fat is called a *simple glyceride*. However, naturally occurring fats contain different fatty acids in the same molecule. These fats are called *mixed glycerides*. Most of the common animal fats are glycerides that contain saturated and unsaturated fatty acids. Since the saturated fatty acids predominate, these fats are solid at room temperature. Beef fat, mutton fat, lard, and butter are important examples of animal fats. Butter fat is readily distin-

guished from other animal fats because of its relatively high content of short chain fatty acids.

Glycerides that are found in vegetables usually exist as oils rather than fats. Vegetable oils such as olive oil, corn oil, cottonseed oil, and linseed oil are characterized by their high content of oleic, linoleic, and linolenic acids. Coconut oil, like butter fat, contains a relatively large percentage of short chain fatty acids.

In addition to their function as foodstuffs and as constituents of protoplasm and body tissues, fats and oils are used in many commercial processes. The manufacture of soap, paint and varnish, oilcloth, linoleum, printing inks, ointments, and creams are a few of their industrial applications.

WAXES

Waxes are simple lipids which are esters of fatty acids and high molecular weight alcohols (other than glycerol). Common naturally occurring waxes are beeswax, lanolin, spermaceti, and carnauba wax. *Lanolin*, from wool, is the most important wax from a medical standpoint, since it is widely used as a base for many ointments and creams. *Spermaceti*, obtained from the sperm whale, is used in cosmetics and some pharmaceutical products, whereas carnauba wax, from the carnauba palm, is used in the manufacture of polishes for floors, furniture, and automobiles.

Paraffin wax, petrolatum, and lubricating oils are not to be confused with the simple lipids discussed above because they are merely mixtures of hydrocarbons.

PHOSPHOLIPIDS

The phospholipids are found in all animal and vegetable cells. They are composed of an alcohol, fatty acids, phosphoric acid, and a nitrogenous base. The three main types of phospholipids are the lecithins, cephalins, and sphingomyelin.

Lecithins

The lecithins are constituents of brain, nervous tissue, and egg yolk. The formula for a typical lecithin may be written as follows:

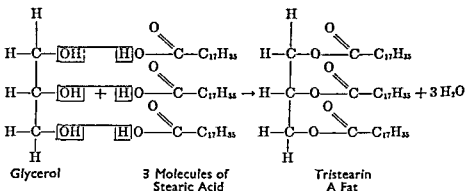
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Sphingomyelin

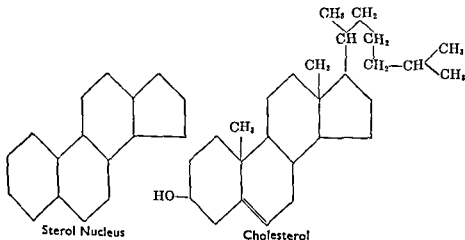
Chemically sphingomyelin differs markedly from the lecithins or cephalins. It is not a glyceride but contains an alcohol called sphingosinol in place of glycerol. Only one fatty acid is present in the molecule, along with phosphoric acid and choline. Sphingomyelin is an essential constituent of brain and nervous tissue and may be used as a source of phosphoric acid in the body.

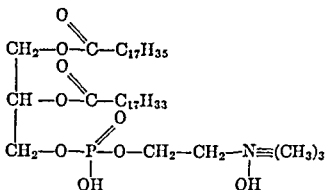
GLYCOLIPIDS

The glycolipids are often called *cerebrosides* because they occur in the brain and nervous tissue. Their structure is similar to the sphingomyelins except that the carbohydrate, galactose, replaces phosphoric acid and choline in the molecule. *Phrenosin* and *kerasin* are the most commonly occurring cerebrosides. It has been suggested that since galactose is an essential constituent of cerebrosides, milk sugar is important in the diet of children during the development of their brain and nervous system.

STEROLS

The sterols are high molecular weight cyclic alcohols that occur in all living cells. The most common sterol is *cholesterol*, which is found in the brain and nervous tissue and in gallstones. Cholesterol and the other sterols are derivatives of the cyclopentanophenanthrene nucleus, also called the sterol nucleus.





A lecithin may be considered as a glyceride in which phosphoric acid has formed an ester with one of the OH groups of glycerol; choline, the nitrogenous base, is joined to the phosphoric acid by a similar ester linkage.

From a physiological standpoint, lecithins are important in the transportation of fats from one tissue to another and serve as a source of phosphoric acid for the synthesis of new cells. In industry, lecithin is obtained from soybeans, and finds wide application as an emulsifying agent. Large quantities of this substance are used in the manufacture of chocolate candies, margarine, aviation gasoline, and medicines.

If the oleic acid on the central carbon atom of lecithin is removed by hydrolysis, the resulting compound is called *lysolecithin*. Disintegration of the red blood cells, or hemolysis, is caused by intravenous injection of lysolecithin. The venom of snakes such as the cobra contains an enzyme capable of converting lecithins into lysolecithins, which accounts for the fatal effects of the bite of these snakes.

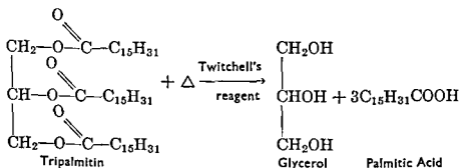
Cephalins

The cephalins are especially abundant in brain tissue. Their chemical composition resembles that of the lecithins except that amino-ethyl alcohol, or cholamine, replaces choline. Cephalin is important in the body because it is one of the factors involved in the blood-clotting process.

formation of acrolein is often used as a test for fats, since all fats yield glycerol when they are heated.

Hydrolysis

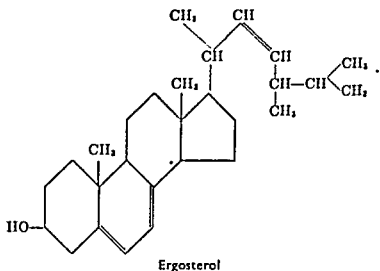
Fats may be hydrolyzed to form free fatty acids and glycerol by the action of acid, alkali, superheated steam, or the enzyme lipase. In hydrolysis of a fat, the three water molecules (that were split out when the three fatty acid molecules combined with one glycerol molecule in an ester linkage to make the fat molecule) are replaced with the resultant splitting of the fat into glycerol and fatty acids. Commercially, fats are a cheap source of glycerol for use in the manufacture of high explosives and pharmaceuticals. For this purpose, the fat is hydrolyzed with superheated steam and *Twitchell's reagent*, which contains naphthalene, oleic acid, and sulfuric acid. The advantage of this method is that glycerol is readily separated from the fatty acids.



Hydrolysis by an alkali is called *saponification*, and produces glycerol and salts of the fatty acids which are called soaps. In the laboratory, fats are usually saponified by an alcoholic solution of an alkali. The fats are more soluble in hot alcohol and the reaction is therefore more rapid.

Rancidity

Many fats develop an unpleasant odor and taste when they are allowed to stand in contact with air at room temperature. The two common types of rancidity are *hydrolytic* and *oxidative*. Hydrolytic changes in fats are the result of the action of enzymes

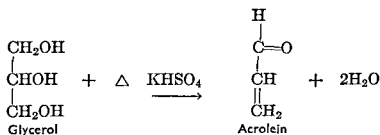


Ergosterol is an important plant sterol that has two more double bonds and one more methyl group than cholesterol. When ergosterol is exposed to ultraviolet light, a mixture of sterols is formed. One of these, called *calciferol*, has vitamin D activity and is administered as a source of this vitamin. Calciferol is also called *drisdol* and, when in an oil solution, is known as *riosterol*. Other substances of physiological importance that contain the sterol nucleus are the bile salts and the sex hormones.

REACTIONS OF FATS

Glycerol Portion

When glycerol or a liquid containing glycerol is heated with a dehydrating agent, *acrolein* is formed.



Acrolein has a very pungent odor and is sometimes formed by the decomposition of glycerol in the fat of frying meats. The

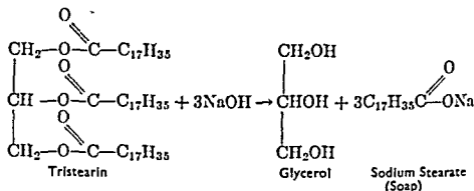
contains no excess alkali and will not harm delicate fabrics. Sodium lauryl sulfate is used as a cleansing agent in toothpastes and powders. Similar substances are employed commercially in Irium and Lusterfoam.

All soaps have mild antiseptic properties; prolonged scrubbing of the hands and arms with soap and water will remove



Fig. 36 An advanced stage of celiac disease. (Courtesy of Dr. P. C. Jeans.)

bacteria from the skin. This procedure is employed by surgeons and nurses when they scrub for an operation. These antiseptic properties are sometimes increased by the addition of mercury compounds or carbolic acid. Zinc stearate is an insoluble soap used in talcum powders for infants because of its antiseptic properties.



Sodium salts of fatty acids are known as *hard soaps*, while potassium salts form *soft soaps*. The ordinary cake soaps used in the home are sodium soaps. Certain cake soaps float because air has been blown into the soap before it is formed into cakes. *Tincture of green soap*, commonly used in hospitals, is a solution of potassium soap in alcohol. When sodium soaps are added to hard water, the calcium and magnesium salts present replace sodium to form insoluble calcium and magnesium soaps. The familiar soap curd formed in hard water is due to these *insoluble soaps*.

Insoluble calcium soaps are found in the feces of children with celiac disease. In this condition, fatty acids are not absorbed from the intestinal tract in a normal manner. The calcium present in the intestine combines with the fatty acid to form insoluble soaps which are subsequently eliminated from the body.

The cleansing power of soaps depends on their ability to lower surface tension and act as emulsifying agents. By emulsifying the grease or oily material that holds the dirt on the skin or clothing, the particles of grease and dirt may be rinsed off with water.

In recent years, an important soap substitute named *gardinol* has been developed. Gardinol is a mixture of the sodium salts of the sulfuric acid esters of lauryl and cetyl alcohols. Gardinol may be used in hard water because it does not form insoluble compounds with calcium and magnesium. The major component of such products as Dreft, Drene, Swerl, Vel, and Tide is gardinol. It is often used to wash silk and woolen material, for it

CHAPTER XV

Proteins

PROTEINS are the most important of the three major foodstuffs (carbohydrates, fats, and proteins). They are found in every living cell of plants and animals and are essential constituents of protoplasm. Many of the tissues of the body such as

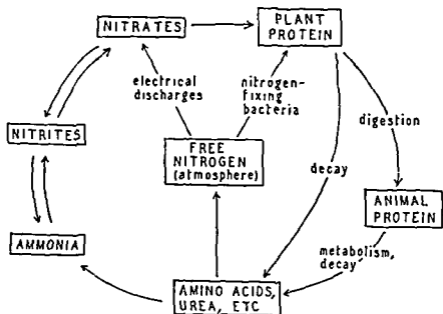


Fig. 37. The nitrogen cycle.

skin, hair, nails, and muscle tissue are especially rich in protein. Normal urine and bile are the only two body fluids that lack protein. Urine is a waste product, and bile functions as an excretory agent to a certain extent.

Proteins are made by plant cells from such simple inorganic

REVIEW QUESTIONS

1. How could you readily distinguish between carbohydrates and lipids in the laboratory?
2. What is meant by the following terms: saturated fatty acid, unsaturated fatty acid, hydroxy fatty acid, and cyclic fatty acid? Give an example of each.
3. Give two examples of the use of fatty acids in medicine.
4. Write the equation for the formation of a fat from palmitic acid and glycerol. What linkage is involved in this process?
5. What is a mixed glyceride? A simple glyceride?
6. List several industrial uses of fats and oils.
7. Distinguish between fats, oils, and waxes. For what purpose are waxes used in medicine? In the home?
8. Compare lecithin and lysolecithin from a chemical standpoint; from a physiological standpoint.
9. What is cephalin? What is its function in the body?
10. How would you define a glycolipid? Why are phrenosin and kersin often called cerebrosides?
11. Write the formula for the sterol nucleus. Name two compounds that contain this nucleus.
12. What relation exists between the sterols and vitamin D? What is calciferol?
13. Which of the following compounds would give a positive acrolein test: fat, phospholipid, sterol? Explain your reasoning.
14. Discuss two methods for the hydrolysis of a fat. What products are formed in each method?
15. What happens when butter becomes rancid? When crackers become stale?
16. What changes in chemical and physical properties take place during the hydrogenation of a vegetable oil?
17. Write an equation to illustrate the saponification of a fat.
18. What are hard soaps, soft soaps, and insoluble soaps? What is tincture of green soap?
19. Give an example of a soap that has antiseptic properties.
20. What advantages do products like Dreft and Tide have over ordinary soaps?



The molecular weight of oxyhemoglobin would thus be about 68,000. The common protein egg albumin has a molecular weight of about 34,500. In general, protein molecules have weights that vary from 34,500 to 50,000,000. Their extremely large size can readily be appreciated when they are compared to the molecular weight of a fat such as tripalmitin which is 807, of sucrose which is 342, or of an inorganic salt such as sodium chloride, which is 58.5.

HYDROLYSIS

In addition to their large size, protein molecules are also very complicated. Like any complex molecule, they may be broken down by hydrolysis into smaller molecules whose structure is more easily determined. Common reagents used for the hydrolysis of proteins are acids (HCl and H_2SO_4), bases (NaOH), and enzymes (proteases). The simple molecules that are formed on the complete hydrolysis of a protein are called *amino acids*. Amino acids are often called the "building stones" used in the construction of the protein molecule. There are about twenty-three amino acids that have been isolated from proteins. Since the smallest naturally occurring protein has a molecular weight of 34,500, it has been estimated that a single protein molecule contains approximately 250 amino acids. The number of possible combinations of the twenty-three different amino acids to form a protein is beyond comprehension. It is therefore impossible to write a structural formula for a molecule so large and complex as the protein molecule.

AMINO ACIDS

Before considering the properties and reactions of proteins, it may be well to study the individual amino acids. An amino acid is essentially an organic acid that contains an amino group. If we replace a hydrogen by an amino group on the carbon atom that is next to the carboxyl group in acetic acid, CH_3COOH , we will form the simple amino acid *glycine*:

substances as carbon dioxide, water, nitrates, sulfates, and phosphates. The complicated synthesis is at present not well understood. Animals are unable to synthesize proteins from inorganic material, so they are dependent on plants or other animals for their source of dietary protein. Proteins are used in the body for growth of new tissue, for maintenance of existing tissue, and as a source of energy. When used for energy, they are broken down by oxidation to form simple substances such as water, carbon dioxide, sulfates, phosphates, and simple nitrogen compounds, which are excreted from the body. These same products are formed in decaying plant and animal matter. The simple nitrogen compounds such as amino acids and urea (Fig. 37), are converted into ammonia, nitrites, and nitrates. The growing plants then use these inorganic compounds to form new proteins and the cycle is completed.

ELEMENTARY COMPOSITION

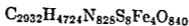
The five elements that are present in all naturally occurring proteins are carbon, hydrogen, oxygen, nitrogen, and sulfur. Small amounts of phosphorus, iron, and iodine are present in some proteins. For example, casein of milk is a phosphoprotein, hemoglobin contains iron, and the protein of the thyroid gland contains iodine. Most proteins show little variation in their elementary composition; the average content of the five main elements is as follows:

ELEMENT	AVERAGE PER CENT
Carbon	53
Hydrogen	7
Oxygen..	23
Nitrogen.	16
Sulfur....	1

The relatively high content of nitrogen differentiates proteins from fats and carbohydrates.

MOLECULAR WEIGHT

Protein molecules are very large, as indicated by the approximate formula for oxyhemoglobin:



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The chemical name for this amino acid would be amino acetic acid. The carbon atom next to the carboxyl group is called the alpha (α) carbon atom, the next one beta (β), the next gamma (γ), and the one farthest from the carboxyl group the eta (ϵ) carbon atom. Since all the amino acids have an amino group attached to the alpha carbon atom, they are known as *alpha amino acids*.

The amino acids are divided into groups according to their chemical structure. Examples of each group are given in the following classification:

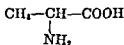
1. Aliphatic amino acids

A. With 1 amino and 1 carboxyl group:

Glycine (amino-acetic acid)

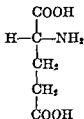


Alanine (α -aminopropionic acid)



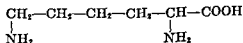
B. With 1 amino and 2 carboxyl groups:

Glutamic acid (α -aminoglutaric acid)

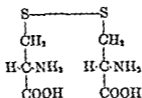


C. With 2 amino and 1 carboxyl group:

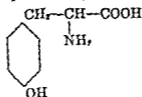
Lysine (α - ϵ -diaminocaproic acid)



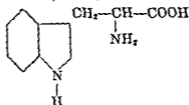
D. Sulfur-containing amino acids:

Cystine di (α -amino- β -thiopropionic acid)

II. Aromatic amino acids

Tyrosine (α -amino- β -parahydroxyphenylpropionic acid)

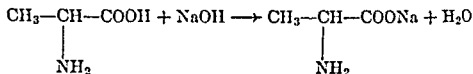
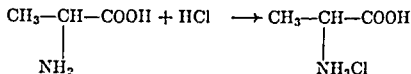
III. Heterocyclic amino acids

Tryptophan (α -amino- β -indolpropionic acid)

In the above classification, the common name of an amino acid is given first, followed by the more complex chemical name. These formulas should help to emphasize the statement that the chemical structure of the protein molecule is complicated.

Amphoteric Property of Amino Acids

The acid properties of an organic acid are due to the carboxyl group, while the basic properties of an organic base are due to the amino group. A compound that contains both of these groups has acidic and basic properties and is said to be *amphoteric*. Amino acids are therefore amphoteric; their amino and carboxyl groups will react with either an acid or a base to form salts. Alanine, which contains one carboxyl and one amino group, will react with an acid and with a base as follows:

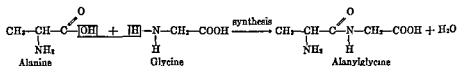


Alanine is neutral to litmus when in a water solution. When an amino acid has 1 amino and 2 carboxyl groups (glutamic acid), its solution is acid, whereas one with 2 amino and 1 carboxyl groups (lysine) forms a solution that is basic to litmus. Since *proteins are made up of amino acids, they are amphoteric substances and are able to neutralize both acids and bases. This amphoteric property of proteins is responsible for their buffering action in the blood and other fluids.*

PROTEIN STRUCTURE

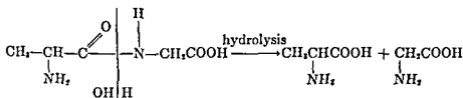
As we have already seen, hydrolysis of proteins results in the formation of α -amino acids. To understand the structure of the protein molecule we must know how the amino acids are joined together to form the large molecules. Several complicated theories have been proposed to explain protein structure. The most reasonable theory, suggested by Emil Fisher, is that amino acids are joined by the peptide linkage.

The *peptide linkage* is formed when the carboxyl group of one amino acid combines with the amino group of another, with the loss of a molecule of water. This type of linkage may be illustrated by the union of a molecule of alanine and a molecule of glycine:



The compound, alanylglycine, which resulted from this linkage, is called a *dipeptide*. The union of three amino acids would result in a *tripeptide*, while the combination of several amino acids by

the peptide linkage would be called a *polypeptide*. Proteins may be considered as complex polypeptides. The above dipeptide may readily be hydrolyzed by the addition of water, to form alanine and glycine:



Complete hydrolysis of a single protein molecule that consisted of 250 amino acids joined together in a long polypeptide chain would require the addition of 249 molecules of water and would result in the formation of 250 individual amino acid molecules.

CLASSIFICATION OF PROTEINS

Proteins are usually divided into three main groups on the basis of their variation in chemical composition. *Simple proteins* are those that yield only amino acids or their derivatives on hydrolysis. The simple proteins are further classified according to their differences in solubility. *Conjugated proteins* are simple proteins combined with some nonprotein compound. The conjugated proteins are named and classified according to the nature of the nonprotein molecule. Several protein classifications include a group called *derived proteins*, which are not naturally occurring proteins and may be considered as protein derivatives that are produced by the action of enzymes, chemical reagents, and various physical forces on simple or conjugated proteins. So many protein derivatives have been reported in the extensive investigations on proteins that an attempt to classify them would only result in confusion. For this reason, the derived proteins are not included in a modern protein classification.

SIMPLE PROTEINS

Albumins

The albumins are soluble in water and are coagulated by heat. Typical albumins are egg albumin in egg white, lactalbumin in milk, and serum albumin in blood.

Globulins

The globulins are insoluble in water, but are soluble in dilute salt solution (such as 5 per cent sodium chloride), and are coagulated by heat. Serum globulin in blood plasma, and lactoglobulin in milk are examples of globulins.

Glutelins

The glutelins are insoluble in water and dilute salt solutions, but are soluble in dilute acid and alkali, and are coagulated by heat. Examples are glutenin in wheat and oryzenin in rice.

Prolamines

The prolamines are soluble in 70 to 80 per cent alcohol, but are insoluble in water or absolute alcohol. Typical prolamines are gliadin in wheat and zein in corn.

Albuminoids

The albuminoids are insoluble in the protein solvents mentioned above and are dissolved only by hydrolysis. The keratin in hair, horn, feathers, and fingernails, and elastin in tendons are examples of albuminoids.

Histones

The histones are soluble in water and dilute acid, but are insoluble in dilute ammonium hydroxide, and are not coagulated by heat. They are slightly basic proteins due to a predominance of the basic amino acids. Examples are the globin in hemoglobin, and thymus histone.

Protamines

The protamines are soluble in water, dilute acid, and dilute ammonium hydroxide, and are not coagulated by heat. They are strongly basic in reaction and are the simplest of all naturally occurring proteins. Salmine and sturine in the sperm of fish are examples of protamines.

CONJUGATED PROTEINS

Nucleoproteins

Nucleoproteins consist of a basic protein combined with nucleic acid. They are present in the nuclei of living cells and are abundantly distributed in glandular tissue.

Glycoproteins

A glycoprotein is the combination of a protein and a carbohydrate. Typical examples are mucin in saliva and mucoids in tendon and cartilage.

Phosphoproteins

Phosphoproteins are proteins that are linked with phosphoric acid. Casein in milk and vitellin in egg yolk are phosphoproteins.

Chromoproteins

The chromoproteins are composed of a protein combined with a colored compound. Examples are hemoglobin in blood and melanin in hair and feathers.

Lecithoproteins

Lecithoproteins are combinations of proteins with lecithin or phospholipids. Thromboplastin in lung tissue is a typical lecithoprotein.

DETERMINATION OF PROTEIN

It is often desirable to know the protein content of various foods and biological material. The analysis of the protein content of such material is based on its nitrogen content. Since the average nitrogen content of proteins is 16 per cent, the protein content of a substance may be obtained by multiplying its nitrogen value by the factor 6.25.

The *Kjeldahl method* is commonly used to determine the amount of nitrogen in organic materials. In brief, the procedure consists of heating the material with concentrated sulfuric acid in the presence of a catalyst (such as a copper or selenium compound). This *digestion process* converts the nitrogen from the

organic form to the inorganic salt, ammonium sulfate. Excess sodium hydroxide is added to the $(\text{NH}_4)_2\text{SO}_4$ and the ammonia that is liberated is distilled into an excess of acid of known concentration. The amount of acid that was neutralized by the ammonia is determined by titration and the amount of ammonia formed is calculated. From this latter value, the nitrogen content of the material can be calculated and, when multiplied by 6.25, gives the protein content of the organic material.

COLOR REACTIONS OF PROTEINS

The color reactions of proteins depend on the presence of certain linkages or specific amino acids in the protein molecules. They are often used to follow the extent of hydrolysis of a protein and for the detection of certain amino acids.

Biuret Test

When a protein solution is mixed with a sodium hydroxide solution and a few drops of a very dilute solution of copper sulfate are added, a violet color is produced. Amino acids and dipeptides do not give the biuret test. A positive test apparently depends on the presence of two or more *peptide linkages*, therefore the biuret test is a good test for proteins or polypeptides. It is often used to follow the hydrolysis of a protein. When the hydrolysate gives a negative biuret test, it can contain only dipeptides and amino acids.

Unoxidized Sulfur Test

We have already seen that naturally occurring proteins contain an average of 1 per cent of sulfur. Part of this sulfur is in the form of the amino acid, *cystine*. When a protein containing cystine is boiled for a few minutes in a solution of sodium hydroxide containing a small amount of lead acetate, the solution turns black. The black color is due to the formation of lead sulfide from the unoxidized sulfur of cystine and the lead of lead acetate.

Millon's Test

Millon's reagent consists of mercuric nitrate and nitrite in a mixture of nitric and nitrous acids. When this reagent is added to a protein solution, the protein precipitates as a mercury salt which turns red when the solution is heated. A positive test is given by any protein that contains *tyrosine*. Millon's test is therefore specific for the amino acid tyrosine in the protein molecule.

Hopkins-Cole Test

A layer of concentrated sulfuric acid is carefully placed under a mixture of a protein and a glyoxylic acid ($\text{CHO}-\text{COOH}$) solution. A violet ring will appear at the zone of contact of the two liquids if tryptophan is present in the protein. The Hopkins-Cole test is thus a test for *tryptophan* in the protein molecule.

Xanthoproteic Test

If concentrated nitric acid is added to a protein solution, the protein first precipitates and then dissolves, forming a yellow color. If the solution is made alkaline with sodium hydroxide, the yellow color changes to an orange. A positive test depends upon the presence of amino acids that contain the benzene ring, such as *tyrosine* and *tryptophan*.

PRECIPITATION OF PROTEINS

One of the most important characteristics of proteins is the ease with which they are precipitated by certain reagents. Many of the normal functions in the body are essentially precipitation reactions, for example, the clotting of blood, or the precipitation of casein by rennin during digestion. Since animal tissues are chiefly protein in nature, however, reagents which precipitate protein will have a marked toxic effect, if introduced into the body. Bacteria, which are mainly protein, are effectively destroyed when treated with suitable precipitants. Many of the common poisons and disinfectants act in this way.

Precipitation reactions are used in clinical and analytical laboratories to identify and separate protein components.

The following paragraphs contain a brief summary of the most common methods of protein precipitation.

By Heat Coagulation

When most protein solutions are heated, the protein becomes insoluble and precipitates, forming coagulated protein. Many protein foods coagulate when they are cooked. Tissue proteins and bacterial proteins are readily coagulated by heat. Routine examinations of urine specimens for protein are made by heating the urine in a test tube to coagulate any protein that might be present.

By Concentrated Inorganic Acids

Proteins are precipitated from their solutions by concentrated acids, such as hydrochloric, sulfuric, and nitric acid. Casein, for example, is precipitated from milk as a curd when acted on by the hydrochloric acid of the gastric juice. A clinical test for protein in urine is known as Heller's ring test. It depends upon the precipitation of any protein present when concentrated nitric acid is added.

By Salts of Heavy Metals

Salts of heavy metals, like mercuric chloride and silver nitrate, precipitate proteins. These salts are used for their disinfecting action and are toxic when taken internally. A protein solution such as egg white or milk, when given as an antidote in cases of poisoning with heavy metals, combines with the metallic salts. The precipitate that is formed must be removed by the use of an emetic before the protein is digested and the heavy metal is set free to act on the tissue protein. A silver salt such as argyrol is used in nose and throat infections, while silver nitrate is used to cauterize wounds and to prevent gonorrheal infection in the eyes of newborn babies.

By Salting Out

Most proteins are insoluble in a saturated solution of a salt such as ammonium sulfate. When it is desirable to isolate a

protein from a solution without appreciably altering its chemical nature or properties, the protein may be precipitated by saturating the solution with $(\text{NH}_4)_2\text{SO}_4$. After filtration the excess $(\text{NH}_4)_2\text{SO}_4$ is usually removed by dialysis. This salting out process finds wide application in the isolation of biologically active proteins.

By Alcohol

Alcohol coagulates proteins other than the prolamines. A 70 per cent solution of alcohol is commonly used to sterilize the skin since it effectively penetrates the bacteria. A 95 per cent



Fig 38 The use of tannic acid in the treatment of burns. (From Christopher, F., Minor Surgery. W. B Saunders Company.)

solution of alcohol is not effective because it merely coagulates the surface of the bacteria and does not destroy them.

By Alkaloidal Reagents

Tannic, picric, and tungstic acids are common alkaloidal reagents that will precipitate proteins from solution. Tannic and picric acids are used in the treatment of burns (Fig. 38). When a solution of either of these acids is sprayed on extensively burned areas, it precipitates the protein to form a protective coating; this excludes air from the burn and prevents the loss of water. In an emergency, strong tea may be used as a source of tannic acid for the treatment of severe burns. Many other therap-

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cutic agents have been used in the treatment of burns, the most recent being penicillin. Nevertheless, considerable quantities of tannic and picric acid preparations are still employed for this purpose. Tungstic and phosphotungstic acids are often used to precipitate the proteins from blood before analyzing the blood for various constituents of clinical importance.

REVIEW QUESTIONS

1. What are the uses of proteins in the body?
2. Briefly explain the fundamental steps in the nitrogen cycle.
3. The presence of what element in proteins differentiates proteins from carbohydrates and fats? What other elements are usually found in proteins?
4. A molecule of egg albumin is approximately how many times as large as a molecule of sucrose?
5. What products result from the complete hydrolysis of a protein? Why would it be difficult to write the structural formula for a protein even though you knew the chemical formulas of the products of hydrolysis?
6. How would you define a protein?
7. What is an amino acid? Write the formulas and names of three amino acids.
8. Why are amino acids classed as amphoteric substances? Would proteins also be amphoteric? Explain.
9. What is the peptide linkage? What simple substance is always split off when the peptide linkage is formed?
10. Illustrate the formation of a tripeptide from three molecules of alanine.
11. Under what three main types are proteins classified? How would you differentiate between the three types?
12. A certain food product was analyzed by the Kjeldahl method and found to have a nitrogen content of 4.0 per cent. What percentage of protein does this food contain?
13. Why is the biuret test used to determine when a protein is completely hydrolyzed?
14. A positive Millon test would indicate the presence of what amino acid in a protein? A positive Hopkins-Cole test?
15. List five important processes involving the precipitation of proteins.
16. How would you treat a patient who had accidentally swallowed a mercuric chloride solution?
17. Describe the action of tannic and picric acids in the treatment of burns

CHAPTER XVI

Enzymes and the Digestive Tract

A MULTITUDE of complex reactions are constantly occurring in the body tissues and in the processes of digestion and metabolism. The speed with which each of these reactions takes place is governed by a catalyst, called an *enzyme*. An enzyme is an organic catalyst that is formed by living cells, but does not require the presence of cells for its action.

The substance on which the enzyme acts is called the *substrate*. The modern system for naming enzymes is to add the ending *-ase* to the root of the name of the substrate. For example, the enzyme that hydrolyzes lipids is called a *lipase* and one that hydrolyzes maltose is called *maltase*. Certain enzymes had common names that had been used for years before this system was introduced. These enzymes retain their original name; for example, pepsin and trypsin are protein-splitting enzymes present in the stomach and intestine respectively. These two enzymes could also be called gastric and intestinal proteases.

CHEMICAL NATURE OF ENZYMES

It is generally accepted at the present time that enzymes are protein in nature. This view is strengthened by the observation that all of the enzymes that have been isolated in a crystalline form are proteins. In general, enzymes in solution are destroyed or inactivated by any treatment that precipitates or coagulates the protein material. Excessive heat, alcohol, salts of heavy metals, and concentrated inorganic acids will rapidly inhibit the activity of an enzyme.

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9. What is the peptide linkage? What simple substance is always split off when the peptide linkage is formed?
10. Illustrate the formation of a tripeptide from three molecules of alanine.
11. Under what three main types are proteins classified? How would you differentiate between the three types?
12. A certain food product was analyzed by the Kjeldahl method and found to have a nitrogen content of 4.0 per cent. What percentage of protein does this food contain?
13. Why is the biuret test used to determine when a protein is completely hydrolyzed?
14. A positive Millon test would indicate the presence of what amino acid in a protein? A positive Hopkins-Cole test?
15. List five important processes involving the precipitation of proteins.
16. How would you treat a patient who had accidentally swallowed a mercuric chloride solution?
17. Describe the action of tannic and picric acids in the treatment of burns

vates it is called a *kinase* or *activator*. The cells of the stomach produce a proenzyme called pepsinogen, which is activated by the hydrochloric acid of the gastric juice. Another proenzyme is trypsinogen that is made in the pancreas and activated in the intestine by enterokinase.

The activity of enzymes is inhibited by any substance that precipitates proteins, such as salts of heavy metals, cyanides, alcohol, and heat. Inhibitors of enzyme action in the body are called *antienzymes*. These substances are believed to be present in the lining of our stomach and intestines to prevent the protein-splitting enzymes from digesting our own tissue. Tapeworms are not digested in the intestine of the host because they are protected by antienzymes in their bodies

CLASSIFICATION OF ENZYMES

Since the reactions of the body are catalyzed by enzymes, there must be different kinds of enzymes to influence the many types of reactions carried out by the body. Enzymes may therefore be classified according to the type of reaction they influence. The most important classes are *hydrolytic enzymes*, which produce hydrolysis of complex molecules; *fermenting enzymes*, which bring about fermentation; *oxidizing* and *reducing enzymes*, which control oxidation and reduction reactions respectively; *deaminizing enzymes*, which form ammonia; and *coagulating enzymes*, which produce coagulation of proteins. Each class may be subdivided into enzymes that act on the various foodstuffs as, for example, the hydrolytic enzymes that hydrolyze carbohydrates, fats, and proteins.

DIGESTION

The majority of the food that is taken into the body is made up of large complex molecules. Before they can be absorbed and utilized by the body they must be broken down into small, relatively simple molecules. The process in which complex food material is changed into simple molecules is called *digestion*. Digestion involves the hydrolysis of carbohydrates into mono-

An important property of an enzyme is that of *specificity* of action. For every reaction that takes place in the body there is a specific enzyme. A lipase will hydrolyze only lipids and has no effect on carbohydrates or proteins. Similarly, maltase attacks only its substrate maltose and will not split sucrose or lactose into their constituent sugars.

FACTORS THAT INFLUENCE THE RATE OF ENZYME ACTION

The rate of enzyme activity is influenced by several factors. The two most important are the temperature and the hydrogen ion concentration of the solution. Other factors that affect the speed of reaction are the concentration of the enzyme and substrate, the nature of the end products, the presence of electrolytes, and light.

The speed of most chemical reactions is increased two or three times for each 10°C . rise in temperature. This is also true for reactions in which an enzyme is the catalyst. Beyond a certain point, however, an increase in temperature will coagulate the enzyme and inactivate it. Every enzyme has an *optimum temperature* at which it exhibits maximum activity. The optimum temperature of the enzymes that are present in the body ranges between 37° and 50°C . (86° and 122°F .).

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ACTIVATION AND INHIBITION OF ENZYMES

Certain enzymes are produced by cells in an inactive form, and require activation by another substance. The inactive form is called a *proenzyme* or a *zymogen* and the substance that acti-

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saccharides, fats into glycerol and fatty acids, and proteins into amino acids by the action of the hydrolytic enzymes.

Many of the changes that take place during the preparation of food may be considered preliminary digestive processes. The cooking of starch aids digestion by rupturing the insoluble amylopectin layer that surrounds the starch granule and by converting the starch into dextrin. The connective tissue of meat is changed into gelatin and the meat is made more tender by cooking.

Storage of meats, fruits, and vegetables often produces a more desirable food due to the action of enzymes during the storage period. Undesirable micro-organisms are often destroyed in the cooking process, thus protecting the body from food poisoning.

Salivary Digestion

Food taken into the mouth is broken into smaller pieces by chewing and is mixed with *saliva*, which is the first of the digestive fluids. The saliva is secreted by three pairs of glands, the parotid, the submaxillary, and the sublingual. It is an almost neutral solution with a pH of about 6.8 and a water content of 99.5 per cent. Saliva contains *mucin*, a glycoprotein which makes the saliva slippery, and *ptyalin*, an enzyme that hydrolyzes starch to maltose. It also contains several inorganic salts such as chlorides and phosphates that are present in the blood.

A normal person secretes approximately 1500 cc. of saliva daily. The flow of saliva is controlled by the nervous system; the sight, odor, or even the thought of food will cause the salivary glands to secrete. The presence of food in the mouth and the mere process of chewing stimulate the flow of saliva.

Ptyalin. Ptyalin is the enzyme responsible for the digestive action of the saliva. It hydrolyzes starch to soluble starch, erythro-dextrin, achroodextrin, and finally maltose. Ptyalin is active over a pH range of 4 to 9 with an optimum pH of 6.6. It is inactivated in the stomach, where the pH may drop to about 1.5. Since this enzyme has little time to act on starches in the mouth, its main activity takes place in the stomach before it is inacti-

COMMON ENZYMES AND THE REACTIONS THEY INFLUENCE

Enzyme	Occurrence	Substrate	End Products
I. <i>Hydrolytic enzymes</i>			
A. Carbohydrases:			
1. Amylases	Saliva	Starch	Dextrins and maltose
Ptyalin	Pancreatic juice	Starch	Maltose
Amylopsin			
2. Sucrase	Intestinal juice	Sucrose	Glucose + fructose
3. Lactase	Intestinal juice	Lactose	Glucose + galactose
4. Maltase	Intestinal juice	Maltose	Glucose + glucose
B. Lipases:			
1. Steapsin	Pancreatic juice	Fats	Fatty acids and glycerol
C. Proteases:			
1. Pepsin	Gastric juice	Proteins	Proteoses and peptones
2. Trypsin	Pancreatic juice	Proteins	Proteoses and peptones and polypeptides
D. Peptidases:			
1. Aminopoly-peptidase	Intestinal juice	Polypeptides	Smaller peptides and amino acids
2. Carboxypoly-peptidase	Pancreatic juice	Polypeptides	Smaller peptides and amino acids
3. Dipeptidase	Intestinal juice	Dipeptides	Amino acids
II. <i>Fermenting enzymes</i>			
1. Zymase	Yeast	Monosaccharides	Ethyl alcohol and carbon dioxide
2. Lactic acidase	Lactic acid bacteria	Lactose	Lactic acid
III. <i>Oxidizing enzymes</i>			
1. Catalase	Plant and animal tissue	Hydrogen peroxide	Oxygen
2. Peroxidase	Plant and animal tissue	Organic peroxides	Oxygen
IV. <i>Deaminizing enzymes</i>			
1. Urease	Animal tissue	Urea	Ammonia and carbon dioxide
V. <i>Coagulating enzymes</i>			
1. Rennin	Gastric juice	Casein	Paracasein
2. Thrombin	Blood	Fibrinogen	Fibrin

There are many small tubular glands located in the walls of the stomach that are responsible for the secretion of *gastric juice*. These glands are stimulated in various ways. The sight, smell, or thought of appetizing foods will cause an increased flow of gastric juice. The presence of food in the stomach is thought to cause the production of a hormone called *gastrin* which diffuses into the blood stream and stimulates secretion by the



Fig. 40. A large gastric ulcer. (From Bockus, H. L. *Gastro-enterology*. Philadelphia, W. B. Saunders Company, Vol 1.)

gastric glands. Gastrin is believed to be identical with *histamine*, which will stimulate the flow of gastric juice when it is injected into the blood stream. The average person secretes 2000 to 3000 cc. of gastric juice a day.

Gastric Juice As secreted, gastric juice is a pale yellow, strongly acid solution containing the enzymes pepsin, rennin, and lipase. The acidity of the gastric juice is due to free hydro-

vated by the acid gastric contents. Food that is well mixed with saliva may undergo salivary digestion for twenty to thirty minutes in the stomach before the ptyalin is inactivated.

The most important functions of saliva are to moisten and lubricate the food for swallowing and to initiate the digestion of starch to dextrins and maltose.

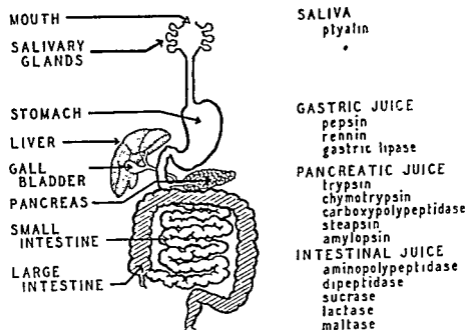


Fig. 39. The digestive system.

Gastric Digestion

When the food is swallowed, it passes through the esophagus into the stomach. The upper end of the stomach, into which the esophagus opens, is called the *fundus*, while the part leading into the intestine is called the *pylorus*. As the food enters the stomach, it distends the muscular wall and collects in the fundic portion. The stomach therefore acts as a storage organ for undigested food. During the process of digestion, the food is mixed with the gastric juice and moves toward the pyloric opening, where it is discharged into the intestine. The food remains in the stomach for one to five hours, depending on the type of meal that is eaten.

1.6 to 1.8. In certain pathological conditions, the acidity of the stomach contents varies considerably. An increase in acidity over the normal is called *hyperacidity*, which is frequently a symptom of gastric ulcers (Fig. 40).

A decrease in acidity is known as *hypoacidity*, a condition commonly associated with cancer (Fig. 41) and anemia. The acidity of the gastric juice is often determined clinically as a diagnostic procedure.

Pepsin is the principal enzyme in the gastric juice. The inactive form, *pepsinogen*, is produced by the cells in the lining of the stomach and is converted into active *pepsin* in the presence of hydrochloric acid. Pepsin acts on the protein in the food, hydrolyzing it into the smaller, more soluble molecules of *proteoses* and *peptones*. The optimum *pH* of pepsin is 1.5 to 2, thus it is ideally suited for the digestion of protein in normal stomach contents, whose *pH* is 1.6 to 1.8.

Rennin is another protease found in gastric juice. It acts on casein, the main protein of milk, changing it into the soluble paracasein. The calcium present in the milk combines with paracasein to form the insoluble calcium paracaseinate curd. This curdling of milk in the stomach is important because the solid material remains in the stomach longer and is acted on by pepsin. Rennin is especially important in the stomach of young mammals whose sole diet is milk.

Gastric lipase is a fat-splitting enzyme that acts on emulsified fats. The acidity of the stomach is unfavorable for the action of lipase and the emulsification of fats, so the amount of fat digested in the stomach is slight. The fats of milk and egg yolk are highly emulsified and may undergo partial hydrolysis in the stomach. As yet it has not been proven whether gastric lipase is formed by the cells of the stomach walls or is present in the stomach because of regurgitation of lipases from the intestine.

Evacuation of the Stomach. As digestion in the stomach proceeds, the food gradually assumes a liquid consistency. The wavelike contractions of the stomach musculature mix the contents with the gastric juice; this liquid mixture is called *chyme*. As the chyme is forced toward the pyloric opening, the pyloric



Fig. 41. Two views of a cancer of the stomach. (From Bockus, H. L.: *Gastro-enterology*. Philadelphia, W. B. Saunders Company, Vol. 1.)

chloric acid, which may be present in a concentration as high as 0.5 per cent. The acidity of the normal stomach contents corresponds to a 0.2 per cent solution of HCl and has a pH of about

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valve relaxes and allows a portion of the stomach contents to pass into the intestine. After the acid chyme is neutralized by the pancreatic juice and bile, another portion of chyme is allowed to pass into the intestine. The time required for gastric digestion and evacuation of the stomach depends on the character of the food that is eaten. A meal which is mainly carbohydrate in nature remains in the stomach about two hours, while a heavy meal of fatty foods and meat remains in the stomach for five hours.

Intestinal Digestion

The acid chyme passes into the small intestine as it leaves the stomach. The first ten inches of the small intestine is known as the *duodenum* and is the most important section from the standpoint of digestion. The next section is called the *jejunum*, while the main portion of the small intestine is known as the *ileum*.

The three digestive juices, namely, the pancreatic juice, intestinal juice, and bile, enter the intestine through the duodenum. These juices are alkaline in reaction and together neutralize the acidity of the chyme.

Pancreatic Juice. The pancreas is a long, glandular organ lying close to the duodenum. Two secretions are formed by the pancreas, an internal secretion called *insulin*, which diffuses into the blood stream and regulates carbohydrate metabolism, and an external secretion called *pancreatic juice* which is carried to the duodenum through ducts. The flow of pancreatic juice occurs only when chyme enters the duodenum. The acid in the chyme converts *prosecretin* in the duodenal wall into *secretin*, a hormone which diffuses into the blood stream. Secretin is thus carried to the pancreas and stimulates the flow of pancreatic juice. Normally about 500 to 800 cc. of pancreatic juice (pH 7.5 to 8) are produced in a day.

Pancreatic Enzymes. There are enzymes present in the pancreatic juice that are capable of digesting proteins, fats, and carbohydrates. The pancreatic proteases are *trypsin*, *chymotrypsin*, and *carboxypolypeptidase*. The first two named are secreted

as the proenzymes, *trypsinogen* and *chymotrypsinogen*. Trypsinogen is activated by the *enterokinase* present in the intestinal juice, while chymotrypsin is activated by trypsin. Both of these enzymes act on native proteins, forming proteoses, peptones, and polypeptides. Trypsin has an optimum pH of 8.2. Chymotrypsin, in particular, possesses the property of clotting milk and may act as a safety factor in infants to take care of any milk that passes through the stomach without being coagulated by rennin. Carboxypolypeptidase further hydrolyzes the polypeptides to form simpler peptides and amino acids.

The pancreatic lipase called *steapsin* hydrolyzes fats into glycerol and fatty acids. The activity of this enzyme is greatly enhanced by the presence of bile, since the bile salts lower the surface tension and cause emulsification of fats.

The pancreatic juice also contains an amylase similar to ptyalin in saliva, called *amyllopsin*. This enzyme splits starch to maltose, with an optimum activity in a neutral to slightly alkaline medium.

The Intestinal Juice. The intestinal juice or *succus entericus* is produced mainly in the duodenum, with smaller amounts being formed in the jejunum and ileum. Although the juice contains enzymes, the main activity is confined to the intestinal mucosa.

Intestinal Enzymes. The most important enzymes present in the intestinal juice are the *peptidases* and the three disaccharide-splitting enzymes, *sucrase*, *lactase*, and *maltase*.

There are two intestinal peptidases: *aminopolypeptidase* hydrolyzes polypeptides to simpler peptides and amino acids, *dipeptidase* hydrolyzes dipeptides to amino acids. These two enzymes therefore complete the hydrolysis of native proteins that has been started by other enzymes. The intestinal peptidases have an optimum pH between 7 and 8.

The three disaccharidases present in intestinal juice account for the hydrolysis of the common disaccharides: sucrose, lactose, and maltose. Cane sugar is the main source of dietary sucrose, milk contains lactose, and maltose comes from the partial hydrolysis of starch by ptyalin and amyllopsin. Sucrase, lactase, and

maltase split these disaccharides into their constituent monosaccharides, thus completing the digestion of carbohydrates.

The Bile. In addition to pancreatic and intestinal juice, bile is poured into the duodenum. Although bile contains no enzymes, it plays an important role in digestion. Bile is formed continuously by the liver; when it is not needed in the intestine it is stored in the gallbladder. Water is absorbed from the bile in the



Fig. 42. A gallbladder packed with gallstones. (From Buckstein, J.: Clinical Roentgenology of the Alimentary Tract, Philadelphia, W. B. Saunders Company.)

gallbladder, concentrating the bile and thus increasing the storage capacity of the gallbladder. When fat enters the small intestine the hormone *cholecystokinin* is liberated into the blood stream, causing the gallbladder to contract and empty the bile into the duodenum. It is estimated that a normal adult produces 500 to 600 cc. of bile per day.

Bile is an alkaline fluid with a yellow-brown to green color

a bitter taste. Its alkaline reaction aids in the neutralization of the acid chyme. From the standpoint of digestion, the *bile salts* are the most important constituents of bile. Several constituents including the *bile pigments* and cholesterol are excreted in the bile.

The Bile Salts. The two most important bile salts are *sodium*

Foodstuff	Digested in	Enzyme	Substrate	End Products
Carbohydrates	Mouth Saliva	Ptyalin	Starch	Dextrins and maltose
	Stomach Gastric juice	No carbohydrate-splitting enzymes		
	Intestine Pancreatic juice	Amylopsin	Starch	Maltose
	Intestinal juice	Sucrase	Sucrose	Glucose and fructose
		Lactase	Lactose	Glucose and galactose
Proteins	Mouth Saliva	Maltase No protein-splitting enzymes	Maltose	Glucose
	Stomach Gastric juice	Pepsin	Proteins	Proteoses and peptones
	Intestine Pancreatic juice	Rennin	Casein	Paracasein
		Trypsin	Proteins, proteoses, peptones	Polypeptides
		Chymotrypsin	Proteins, proteoses, peptones	Polypeptides
	Intestinal juice	Carboxypolypeptidase	Polypeptides	Peptides and amino acids
		Aminopolypeptidase	Polypeptides	Peptides and amino acids
Lipids	Mouth Saliva	Dipeptidases No lipid-splitting enzymes	Dipeptides	Amino acids
	Stomach Gastric juice	Gastric lipase	Emulsified fats	Fatty acids and glycerol
	Intestine Pancreatic juice	Steapsin	Fats	Fatty acids and glycerol

glycocholate and *sodium taurocholate*. As mentioned previously, they are compounds that contain the sterol nucleus. Their main function in digestion is the emulsification of fats, which they accomplish by lowering the surface tension. The activity of the pancreatic lipase, steapsin, is greatly increased in the presence of bile salts. By increasing the speed with which fats are digested, they also indirectly assist in the digestion of proteins and carbohydrates; for if a considerable portion of the meal consists of fatty foods, the fat tends to coat the other food particles and must be removed before the other enzymes can act.

The Bile Pigments. When red blood cells decompose, hemoglobin is oxidized to form *bilirubin*, which is excreted into the bile by the liver. Bilirubin is the main bile pigment and is reddish in color. On oxidation it is converted into the green pigment *biliverdin*, while on reduction it forms the brown *stercobilin*. Stercobilin is the normal pigment of the feces. Bilirubin is also reduced to form *urobilin*, which may be reduced to form *urobilinogen*. The chief pigment of the urine, called *urochrome*, is a mixture of urobilin and urobilinogen.

In cases of obstruction of the bile duct or impairment of the liver, there is an accumulation of bile pigments in the blood and the skin becomes yellow. This condition is called *jaundice*. The black and blue spot caused by an injury is a visual demonstration of the conversion of hemoglobin into bile pigments.

Cholesterol. This common sterol is excreted from the body by way of the bile. When the bile is concentrated in the gallbladder the cholesterol sometimes precipitates around a foreign body to produce *gallstones*. A gallbladder filled with gallstones is shown in Fig 42. Although there are other types of gallstones, the most common type formed in the human gallbladder is composed mainly of cholesterol.

Functions of Bile. The functions of bile may be summarized as follows: (1) it aids in the neutralization of the acid chyme, (2) it emulsifies and promotes solution of the fats, (3) it activates steapsin and accelerates its action, (4) it dissolves the insoluble fatty acids and assists in the absorption of fats, (5) it reduces intestinal putrefaction by stimulating peristalsis.

Summary

The digestion of the three major foodstuffs as they pass down the alimentary canal is outlined in the table on page 197.

ABSORPTION

The passage of the end products of digestion through the walls of the small intestine into the blood and tissues is called *absorption*. No food material is absorbed from the mouth and very little is absorbed from the stomach.

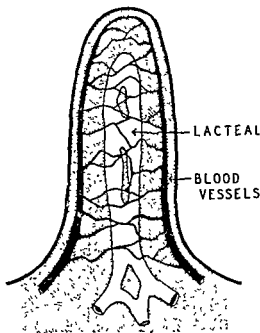


Fig. 43. A diagram of a villus

The small intestine is especially adapted for absorption. Although the superficial surface area measures about $\frac{1}{2}$ square meter, the effective absorbing surface is nearly 10 square meters because of the folds in the mucous lining and the numerous finger-like projections called *villi*. The food usually remains in the small intestine from four to six hours for the process of intestinal digestion and absorption to take place. During this period, the end products of digestion are absorbed through the villi into the blood or lymph stream. The human small intestine

contains from 4,000,000 to 5,000,000 villi. Each villus (Fig. 43) consists of a lining of cells that surround a central *lacteal* or lymph capillary. A network of blood capillaries surrounds the lacteal, thus providing a rapid circulation of blood close to the surface. The blood and lymph capillaries from several villi coalesce to form larger blood and lymph vessels.

Absorption of Carbohydrates

When the digestive process is completed, the carbohydrates exist as the monosaccharides glucose, fructose, and galactose. These monosaccharides are absorbed directly into the blood stream through the capillary blood vessels of the villi. They are carried by the blood to the liver, where they are converted into *glycogen* for storage and for subsequent conversion to glucose.

Absorption of Fats

The end products of fat digestion are glycerol and fatty acids. These compounds are absorbed into the lacteals of the villi and appear in the lymph stream as resynthesized fat. The glycerol and fatty acids are probably built into phospholipid molecules for their transportation through the intestinal wall. Immediately after their passage through the wall, the phospholipid apparently releases the glycerol and fatty acids, which then recombine to form fat molecules. The fat in the lymph is carried through the larger lymphatics to the thoracic duct, from which it enters the blood stream and is carried to the tissues and fat depots. One of the major functions of the bile salts is to assist in the absorption of the fatty acids and glycerol by dissolving the fatty acids, which are insoluble in water.

Absorption of Proteins

The complete digestion of proteins yields amino acids, which are absorbed directly into the blood stream. The amino acids are carried to the tissues where they are used for building new tissue or are oxidized to produce energy. The body does not contain storage depots for protein as it does for fats and carbohydrates.

FORMATION OF FECES

The intestinal contents are still fluid as they leave the ileum and pass through the ileocecal valve into the large intestine. They consist mainly of undigested food residues, remains of digestive and intestinal secretions, and cellular debris. This material normally remains in the large intestine for one to two days, where it is converted into feces by the reabsorption of water. In addition to the food residues, the feces contain bile salts, bile pigments, mucin, sterols, and inorganic salts. Approximately one-fourth or more of the feces consist of bacteria.

The character of the feces does not depend entirely on the nature of the diet. An exclusive carbohydrate diet will produce feces with a composition similar to that produced on an exclusive protein diet. Starvation does not markedly alter the composition of the feces, so the feces must be derived mainly from secretions of the alimentary tract. Foods that contain a high percentage of cellulose produce a bulky feces. From 25 to 50 gm. of dry fecal matter are excreted per day on a normal mixed diet.

BACTERIAL ACTION IN THE INTESTINE

Increasing numbers of bacteria are found in the lower section of the small intestine, and they make up a considerable portion of the total contents of the large intestine. In certain animals such as cows, sheep, and horses, the intestinal bacteria play an active role in the digestion of cellulose. By splitting cellulose into simpler carbohydrates, they make available food material otherwise indigestible by ordinary enzymes.

The two main types of bacterial action in the human intestine are *fermentation* of carbohydrates and *putrefaction* of protein material. If any of the simple carbohydrates have escaped digestion or absorption, they undergo fermentation to form gases (hydrogen, carbon dioxide, and methane) and acids (acetic, lactic, and butyric). The gases may cause distention of the intestinal tract and the acids may cause diarrhea in infants by irritating the intestinal mucosa. Fermentative diarrhea in infants is often treated by decreasing the carbohydrate in their formula or by feeding milk of high protein and low carbohydrate content.

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Absorption of Fats

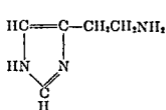
The end products of fat digestion are glycerol and fatty acids. These compounds are absorbed into the lacteals of the villi and appear in the lymph stream as resynthesized fat. The glycerol and fatty acids are probably built into phospholipid molecules for their transportation through the intestinal wall. Immediately after their passage through the wall, the phospholipid apparently releases the glycerol and fatty acids, which then recombine to form fat molecules. The fat in the lymph is carried through the larger lymphatics to the thoracic duct, from which it enters the blood stream and is carried to the tissues and fat depots. One of the major functions of the bile salts is to assist in the absorption of the fatty acids and glycerol by dissolving the fatty acids, which are insoluble in water.

Absorption of Proteins

The complete digestion of proteins yields amino acids, which are absorbed directly into the blood stream. The amino acids are carried to the tissues where they are used for building new tissue or are oxidized to produce energy. The body does not contain storage depots for protein as it does for fats and carbohydrates.

- 3 What two factors have a strong influence on the rate of action of an enzyme?
- 4 Define optimum pH; optimum temperature Give the optimum pH and optimum temperature of two enzymes.
- 5 What explanation would you give for the formation of enzymes in an inactive state by the cells?
- 6 List five general types of enzymes. Which type is the most important in digestion? Why?
- 7 How would you define digestion? What reaction always occurs in the digestion of food?
- 8 What are the main functions of saliva?
9. What enzyme is present in the saliva? Upon what substrate does it act?
10. Does salivary digestion occur to any extent in the stomach? Explain.
11. What characteristic of gastric juice distinguishes it from all other fluids in the body?
12. What abnormal conditions are frequently associated with hyperacidity of the gastric juice? With hypoacidity?
13. List the principal enzymes of the gastric juice with their substrates and end products of digestion
14. Why is rennin most important in infant nutrition?
15. What is chyme? How is it formed?
- 16 How is the flow of pancreatic juice controlled?
17. Name the protein-splitting enzymes of the pancreatic juice.
- 18 Discuss two of the differences between pancreatic and intestinal juices.
- 19 List the important characteristics and composition of bile.
20. Why are the bile salts of importance in digestion?
21. Describe three locations in the body where you might observe bile pigments.
22. How are gallstones usually formed? What constituent predominates in gallstones?
- 23 List the important functions of bile.
- 24 What is absorption? In what part of the alimentary canal does it occur?
- 25 Why are the villi important in the process of absorption?
26. Describe briefly the absorption of carbohydrates, fats, and proteins
27. What type of material is present in the feces?
- 28 What causes fermentative diarrhea in infants? How is it treated?

Putrefaction of protein material in the large intestine results in the formation of products that may be toxic if absorbed into the blood stream. The bacteria split the proteins into amino acids, which they further decompose by the removal of carbon dioxide or ammonia. Some typical products of intestinal putrefaction are histamine, phenol, indole, and skatole. Histamine has



Histamine



Phenol



Indole



Skatole

marked physiological properties, while indole, and skatole are responsible for the characteristic odor of the feces. Small amounts of these toxic compounds may be absorbed from the intestine and carried by the blood to the liver where they are detoxified. Indole, for example is converted into nontoxic indican which is excreted in the urine. An abnormally large excretion of indican in the urine would indicate that excessive putrefaction was occurring in the large intestine.

Symptoms such as headaches, drowsiness, mental depression, and general malaise that accompany constipation have been attributed to the absorption of toxic compounds from the intestine. At the present time, it is considered that these symptoms are not caused by intestinal putrefaction. It should be kept in mind that a certain amount of intestinal putrefaction occurs normally and that mechanisms are present in the body to take care of these toxic products. If it is desirable to reduce the extent of putrefaction in the intestine, a high carbohydrate and low protein diet is beneficial.

REVIEW QUESTIONS

1. What is an enzyme? A substrate? Give two examples of enzymes and their substrates
2. Why should enzyme solutions not be boiled or treated with alcohol or concentrated acids?

are available to counteract changes in the blood sugar level. After an ordinary meal, the glucose in the blood reaches ~~hyperglycemia~~

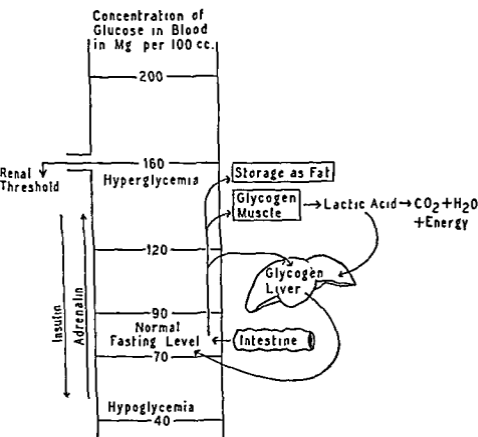


Fig. 44. The factors that regulate the glucose levels in the blood. (Adapted from Bodansky, M.: *Introduction to Physiological Chemistry*. 4th ed. New York, John Wiley & Sons, Inc.)

glycemic levels; this may be returned to normal by the following processes:

1. Storage
 - (a) as glycogen
 - (b) as fat
2. Oxidation to produce energy
3. Excretion by the kidneys

The operation of these factors in counteracting hyperglycemia is illustrated by the diagram in Fig. 44. The space between

CHAPTER XVII

Carbohydrate Metabolism

ALL of the chemical changes that occur in the tissues after absorption of food molecules takes place are known as *metabolism*. Metabolism is usually divided into two types of changes, namely, *anabolism* and *catabolism*. Anabolism is the "building-up process" which is responsible for the formation of new tissue, repair of old tissue, and the synthesis of substances such as enzymes and hormones. Catabolism, the opposite of anabolism, is the "breaking-down process" involved in the conversion of body tissues or foods into energy and waste products.

THE BLOOD SUGAR LEVEL

The main end products of carbohydrate digestion in the body are the three important monosaccharides, glucose, fructose, and galactose. These sugars are absorbed into the blood stream and are carried by the portal circulation to the liver. Fructose and galactose are converted into glucose by the liver cells. The metabolism of carbohydrates therefore is essentially the metabolism of glucose.

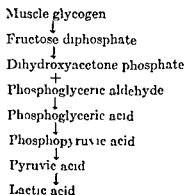
The concentration of glucose in the general circulation is normally 70 to 90 mg. per 100 cc. of blood. This is known as the *normal fasting level* of blood sugar. After a meal containing carbohydrates, the glucose content of the blood increases, causing a temporary condition of *hyperglycemia*. In cases of severe exercise or prolonged starvation, the blood sugar value may fall below the normal fasting level, resulting in the state of *hypoglycemia*. One of the major functions of the tissues is to maintain blood of a constant composition, therefore several mechanisms

OXIDATION OF CARBOHYDRATES

Glucose is ultimately oxidized in the body to form carbon dioxide and water with the liberation of energy. However, this process is complicated by the formation of several intermediate products whose interrelationships are not clearly defined. Although oxidation of glucose occurs in the various tissues of the body, our information is largely confined to the process in the muscles.

Much study has been devoted to the chemical changes which occur when carbohydrates are metabolized in the muscle. It has been known for many years that one of the products of muscular activity is lactic acid. About four-fifths of the lactic acid that is formed in muscular contraction is changed back to glycogen in the muscle, or is carried as blood lactic acid to the liver, where it is converted into liver glycogen. The other fifth of the lactic acid is oxidized to carbon dioxide and water.

Muscle glycogen is apparently the source of energy for muscular activity. The first reaction is probably the hydrolysis of glycogen to form a hexose sugar. The hexose sugar then combines with two molecules of phosphoric acid to form a hexose diphosphate which is split into two triose monophosphates. The triose monophosphates are rearranged with the ultimate formation of pyruvic acid, which is then converted into lactic acid. The intermediate compounds which are thought to be involved in the oxidation of glycogen in the muscle are shown in the following outline:



the vertical lines may be compared to a thermometer with values expressed as milligrams of glucose per 100 cc. of blood. During active absorption of carbohydrates from the intestine, the blood sugar level rises, causing a temporary hyperglycemia. In an effort to bring the glucose concentration back to normal, the liver may remove glucose from the blood stream, converting it into glycogen for storage. The muscles will also take glucose from the circulation to convert it to glycogen or to oxidize it to produce energy. If the blood sugar level continues to rise, the glucose may be converted into fat and stored in the fat depots. These four processes usually control the hyperglycemia; however, if large amounts of carbohydrates are eaten and the blood sugar level exceeds 160 mg. of glucose per 100 cc., the excess is excreted by the kidneys. The blood sugar level at which the kidney starts excreting glucose is known as the *renal threshold* and has a value from 150 to 170 mg. per 100 cc.

Since carbohydrate metabolism is essentially the regulation of the blood sugar level, we will discuss the above factors in detail.

GLYCOGEN FORMATION

During absorption of the carbohydrates, the excess glucose is stored as glycogen in the liver. Normally this organ contains about 100 gm. of glycogen but may store as much as 400 gm. The glycogen in the liver is readily converted into glucose and serves as a reservoir from which glucose may be drawn if the blood sugar level falls below normal. The formation of glycogen from glucose is called *glycogenesis*, while the conversion of glycogen to glucose is known as *glycogenolysis*. The muscles also store glucose as glycogen, but muscle glycogen is not as readily converted into glucose as is liver glycogen.

Substances other than the carbohydrates in food may be converted into glycogen. About 58 per cent of the amino acids from protein digestion, the glycerol portion of fats, and lactic acid from the contraction of muscles will form glycogen. These substances, therefore, contribute to the glucose supply of the body when they are needed.

increase in the blood sugar level. Glucose is usually excreted in the urine because the renal threshold is exceeded. The impairment of carbohydrate oxidation causes the formation of an excess of ketone bodies. Many of these ketone bodies are acid in nature, and the severe acidosis that results from the lack of insulin causes *diabetic coma*, which is often fatal to a diabetic patient. When insulin is injected, carbohydrate metabolism is properly regulated and the above symptoms do not appear.

A more detailed description of diabetes will be presented in the chapter on hormones (Chap. XXIV).

Epinephrine (Adrenalin)

This substance is produced by the adrenal glands. It is antagonistic to the action of insulin in that it causes glycogenolysis in the liver with liberation of glucose. Continued secretion of epinephrine occurs under the influence of strong emotions such as fear and anger. In these cases, the epinephrine liberates glucose from liver glycogen and increases the blood sugar level. This mechanism is often used as an emergency function to provide carbohydrate for muscular work. The hyperglycemia that results often exceeds the renal threshold, and glucose is excreted in the urine.

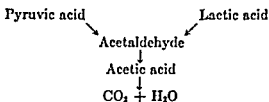
GLUCOSE TOLERANCE

Glucose Tolerance Test

The capacity of the body to assimilate large doses of glucose, without excreting sugar in the urine, has long been of clinical interest. This glucose tolerance is a valuable aid in the diagnosis of diabetes. The blood of a fasting person is analyzed for glucose. Then 50 to 100 gm. of glucose are administered by mouth and the glucose concentration is determined at intervals. The blood sugar level of a normal person will rise to a maximum during the first half-hour or hour interval and will return to approximately the normal fasting level at the end of two hours.

The rapid absorption of the ingested glucose apparently causes the pancreas to secrete insulin, which removes glucose from the blood until the normal level is reached. A diabetic

To complete the oxidation of carbohydrates in the body, pyruvic acid and the one-fifth of the lactic acid that is not converted to liver glycogen are oxidized as follows:



CONVERSION OF CARBOHYDRATE TO FAT

It is a common observation that persons who consume an excessive amount of carbohydrates in their diet become fat. The body is able to convert carbohydrates into fat, but the mechanism for this change is not clear. The glycerol portion of a fat could easily be formed from glyceric aldehyde, which is an intermediate product in carbohydrate metabolism, by reduction of the aldehyde group to an alcohol. The long-chain fatty acids may possibly be built by the condensation of several molecules of a simple unit such as acetaldehyde, which contains two carbon atoms.

THE ACTION OF INSULIN AND EPINEPHRINE

Insulin

Insulin is a hormone that is formed by the pancreas. It is an essential factor in carbohydrate metabolism and is responsible for the regulation of the normal blood sugar level. The main functions of insulin are as follows:

1. It is necessary for the conversion of glucose into liver and muscle glycogen for storage.
2. It is necessary for the proper oxidation of carbohydrates in the body.
3. It prevents the breakdown of glycogen to glucose in the liver.

Diabetes Mellitus. If the pancreas fails to produce sufficient insulin, a condition of *diabetes mellitus* results. The failure of the storage mechanisms in the absence of insulin causes a marked

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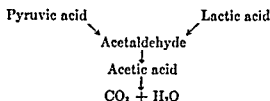
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Phlorhizin Diabetes. Glycosuria may also be caused by the injection of the drug, phlorhizin, into experimental animals. This condition is called phlorhizin diabetes and is often used to study some of the factors in diabetes.

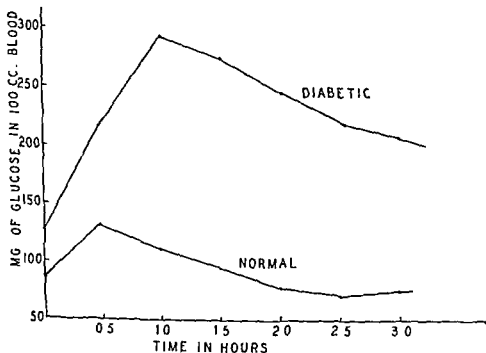


Fig. 45 Glucose tolerance curves.

False Glycosuria. A positive Benedict's test may be observed on urine specimens in the last stage of pregnancy and during lactation. This is due to the presence of lactose in the urine, and is called false glycosuria.

REVIEW QUESTIONS

1. Explain the meaning of the terms: metabolism, anabolism, and catabolism.
2. Why is the metabolism of carbohydrates essentially the metabolism of glucose?

person, lacking this controlling effect, cannot tolerate the large dose of glucose. The blood sugar level of the diabetic person would be higher at the start of the test and would probably reach a peak at the end of the first hour interval. The original level would not be reached for several hours, and large quantities of glucose would appear in the urine. The chart in Fig. 45 illustrates the difference between glucose tolerance curves obtained from a normal and a diabetic patient.

Excretion of Glucose

Any condition which produces a hyperglycemia in excess of 180 mg. per 100 cc. of blood will result in the appearance of glucose in the urine. The kidney may be compared to a dam that holds back the glucose of the blood stream until it rises beyond the top of the dam and spills over into the urine. The renal threshold may be considered as the top of the dam. The blood sugar level of a patient with uncontrolled diabetes is usually above the renal threshold, causing glucose to be spilled into the urine almost continuously. It is not unusual for such a patient to excrete 200 to 300 gm. of glucose in the urine per day. In a completely diabetic patient, the main mechanism for removing glucose from the blood is that of excretion by the kidney.

The presence of appreciable amounts of glucose in the urine is known as *glycosuria*. When a routine examination of a urine specimen reveals a positive Benedict's test, diabetes is usually suspected. However, there are several other conditions that may cause glycosuria and these may be outlined as follows:

Alimentary Glycosuria. This is a transitory type of glycosuria that results from the ingestion of a large quantity of sugar. The sugar is absorbed so rapidly that the body is unable to convert it into glycogen fast enough to maintain a blood sugar level below the renal threshold. After the excess sugar is excreted, the level returns to normal.

Renal Diabetes. Glucose is excreted in the urine in renal diabetes because the renal threshold of the person is abnormally low; thus glucose is excreted even when the blood sugar level is normal.

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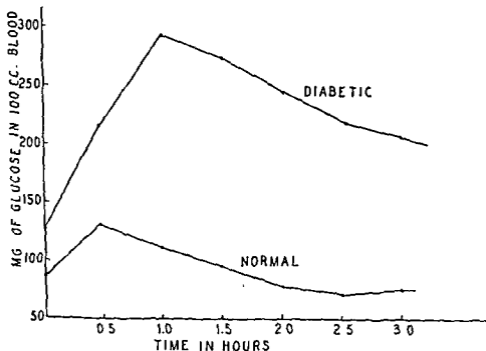


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CHAPTER XVIII

Fat Metabolism

THE end products of fat digestion are fatty acids and glycerol, which are absorbed into the lymph stream. During their passage through the intestinal wall, they are resynthesized into fat molecules. The fat is carried by the lymph circulation to the thoracic duct, where it is poured into the blood stream. After a meal containing fat, the fat content of the blood increases.

UTILIZATION OF FATS

The increased amount of fat that is present in the blood stream after a meal is utilized by the body in the following ways:

1. Synthesis of complex lipids
2. Storage
3. Oxidation to furnish energy

Synthesis of Complex Lipids

Certain lipids are essential constituents of protoplasm and are probably synthesized from fats of the food. Phospholipids such as sphingomyelin and lecithin are necessary in the formation of brain and nervous tissue. Lecithin is used in transporting fats to the various tissues and may be involved in the oxidation of fats. Another essential phospholipid is cephalin, which is a vital factor in the clotting of blood. Special fats and oils in the body, such as the natural oil of the scalp and the wax of the ear, are examples of lipids synthesized from the fat of the food.

Storage

Fats may be removed from the blood stream by storage in the various fat depots. When fat is stored under the skin, it is

3. How would you designate the following glucose concentrations in the blood: 150 mg. per 100 cc., 80 mg. per 100 cc., and 50 mg. per 100 cc.?
4. What are the factors that maintain the glucose concentration of the blood at a fairly constant level?
5. How could you represent glycogenesis and glycogenolysis in one simple equation? Of what importance are these processes in carbohydrate metabolism?
6. What happens to the lactic acid that is formed by carbohydrate metabolism in the muscles?
7. If the pancreas were unable to form insulin, what alterations would occur in carbohydrate metabolism?
8. Why is epinephrine considered antagonistic to the action of insulin? In what condition would this be advantageous?
9. What is meant by the statement that a diabetic cannot tolerate large doses of glucose by mouth?
10. Define the terms: glycosuria, renal threshold, and diabetes mellitus.
11. Glucose is sometimes excreted in the urine of apparently normal persons. Name three conditions that might result in this glycosuria. Explain each briefly.

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Storage

Fats may be removed from the blood stream by storage in the various fat depots. When fat is stored under the skin, it is

usually called *adipose tissue*. However, considerable quantities of fat may be stored around such organs as the kidneys, heart, lungs, and spleen. This type of depot fat acts as a support for these organs and helps to protect them from injury.

The composition of the storage fat is generally characteristic for a given species of animal. If large amounts of fat are fed to an animal, the nature of the stored fat will be similar to that of the dietary fat. This may produce an undesirable fat from a commercial standpoint, for example the fattening of hogs for market. Southern hogs that are fed cottonseed oil and peanut oil develop a soft storage fat that produces inferior bacon and hams. These hogs are often fed more saturated fats shortly before they are sold, in order to harden their storage fat.

Obesity. Obesity is the condition in which excessive amounts of fat are stored in the fat depots. In a small percentage of cases, obesity is due to a disorder of certain endocrine glands, but as a general rule it results from eating more food than the body requires. Most of the food consumed by an adult is used to produce energy, and food in excess of that necessary to fulfill the energy requirements of the body is stored as fat. Thin people generally are more active than fat people and are able to eat larger amounts of food without putting on weight.

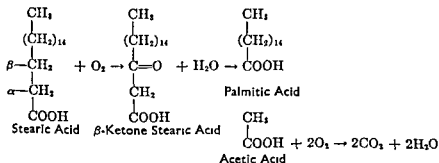
Many people apparently eat all they want and yet maintain a fairly constant weight over long periods of time. This weight control may be due to the appetite, which is abnormally increased in people that are gaining weight and decreased in those who are losing weight. Many experiments have shown that the law of conservation of energy operates in this connection. A thin person can be made to gain weight by feeding him more food than he needs, whereas a fat person can lose weight by eating less than his energy requirements call for.

Oxidation of Fats

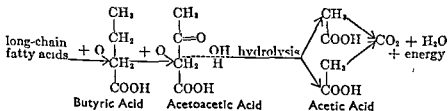
Since fats are converted into phospholipids for transportation in the blood stream, it is probable that the food or storage depot fat is presented to the tissues for oxidation in this form. The first step in the oxidation process is the hydrolysis of the phospholipid into glycerol and fatty acids. The glycerol is oxi-

dized to glyceric aldehyde, which is an intermediate compound in carbohydrate metabolism, and thus enters the chain of reactions involved in the oxidation of carbohydrates. The fatty acids are oxidized to form carbon dioxide and water and a relatively large amount of energy. The oxidation of a gram of fat will produce more than twice the amount of energy obtained from the oxidation of a gram of carbohydrate or protein.

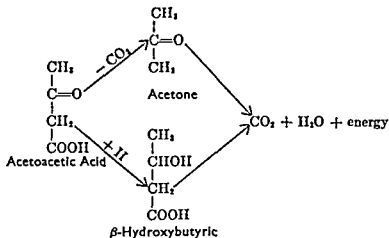
The intermediate steps in the oxidation of fatty acids in the tissues are not definitely known, although *Knoop's theory of beta-oxidation* is generally accepted as an explanation of the mechanisms. Knoop believed that the long-chain fatty acids were oxidized at the beta-carbon atom, forming a ketone group, after which the end two carbon atoms were split off, leaving a fatty acid with two less carbon atoms. It may be recalled that the α -carbon atom is next to the carboxyl group, thus the β -carbon atom would be next to the α -carbon atom. The oxidation of stearic acid to form palmitic acid may be illustrated as follows:



The palmitic acid may then be oxidized in a similar manner to form myristic acid (with 14 C atoms) and another molecule of acetic acid. The process of oxidation continues until butyric acid is formed. The butyric acid is oxidized to acetoacetic acid, acetic acid, then carbon dioxide and water as shown:



In the liver, *acetoacetic acid* in addition to forming acetic acid is also converted into *acetone* and β -*hydroxybutyric acid* as follows:



The above three compounds, acetoacetic and β -hydroxybutyric acids, and acetone are known as the *acetone bodies*. For many years it was thought that the acetone bodies were products of abnormal metabolism, especially since they accumulated in the blood and were excreted in the urine in diabetes and in starvation. The modern viewpoint is that the acetone bodies are normally produced by the liver during metabolism of the fatty acids. The liver cannot oxidize them to CO_2 , H_2O , and energy, but this process takes place in the muscle tissue. Under ordinary conditions when the body is metabolizing carbohydrates, fats, and proteins, the fatty acids and the acetone bodies that are formed are completely burned to CO_2 , H_2O , and energy. During starvation when carbohydrates are lacking or in diabetes when they are not properly utilized, the body must metabolize larger quantities of fats and proteins. Under these conditions the liver may produce more acetone bodies than the muscles can oxidize, thereby causing an accumulation in the blood and subsequent excretion in the urine. Acetone, being a volatile substance, may also be excreted by the lungs and is responsible for the fruity odor of the diabetic person's breath. The two acids neutralize the alkali of the blood and tissues and cause acidosis.

Severe diabetes or prolonged starvation may result in the formation of such large quantities of these acids that the alkali reserve of the blood is lowered to a point where the patient goes into a coma from the acidosis. This *diabetic coma* is sometimes fatal.

REVIEW QUESTIONS

1. How does the body bring the fat concentration of the blood back to normal after a meal containing fat?
2. Which process for the utilization of fat by the body would you consider the most important? Explain.
3. Name four special lipids that must be synthesized from the fat in the diet.
4. Why is a certain amount of depot fat desirable in the body?
5. What method would you prescribe for a rapid reduction of excess body weight? What two principles are important in reducing?
6. Outline Knoop's theory of beta-oxidation.
7. Write an equation for the beta-oxidation of butyric acid to form acetic acid.
8. Why are acetone bodies often found in the urine of persons on drastic reducing diets?
9. What are the acetone bodies? Where are they formed?
10. Write an equation for the formation of acetone bodies from acetoacetic acid.
11. Why should an excess formation of acetone bodies result in a condition of acidosis?
12. What happens to the acetone bodies that are formed in the liver of a normal person?

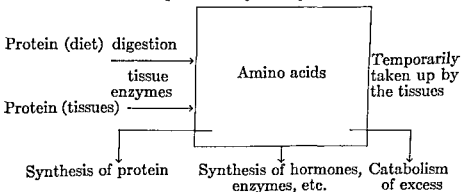
Protein Metabolism

WHEN proteins are digested, they are broken down into their amino acids, which are absorbed into the blood stream. The amino acids are carried by the portal circulation to the liver and are then distributed to the tissues of the body. There are no storage depots for amino acids or proteins as there are for fats and carbohydrates. Therefore the amino acids coming into the blood stream after a meal are either utilized by the body or oxidized to produce energy.

UTILIZATION OF PROTEINS

Amino acids from the protein of the diet or from the breakdown of tissue proteins are temporarily taken up by the tissues before being used by the body. From this pool of amino acids, the body draws its building stones for the construction of new tissue for growth, or for the synthesis of biologically active substances such as hormones and enzymes. Any excess that is left after these requirements are met undergoes catabolism to form energy and the end-products of protein metabolism.

The utilization of protein may be represented as follows:



These processes will be discussed in the order of their importance to the body.

Synthesis of Protein

Growing children require large quantities of amino acids to build new tissue. The body apparently selects the proper assortment of amino acids from those temporarily stored in the tissues to construct the different proteins that are needed for the growth of various organs and muscle tissue.

The situation is somewhat different in adults. If they are neither gaining nor losing weight, the amino acids necessary for growth of new tissue are negligible. A small quantity of amino acids, however, is constantly required for the repair of body tissues. Continued muscular exercise will result in the formation of new muscle tissue, which will require amino acids; in general, however, the requirement of amino acids for the synthesis of new protein tissue in an adult is very small.

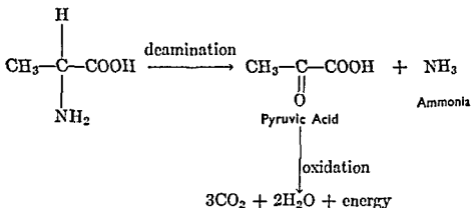
Synthesis of Hormones and Enzymes

The protein nature of enzymes is well accepted, and a supply of amino acids must be present for their synthesis. Several hormones are known to be protein in nature. Since hormones are synthesized in certain endocrine glands, a supply of amino acids must be made available to these glands. Insulin, the hormone made by the pancreas, is probably synthesized from a combination of amino acids different from that used for tissue protein or enzymes. The glands or tissues that manufacture certain hormones and enzymes must have the property of selecting the correct proportions of each amino acid to build a protein molecule characteristic of that gland or tissue.

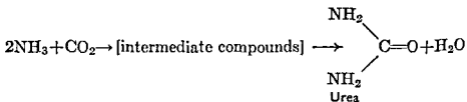
Catabolism of Protein

The excess amino acids that are not used for synthesis of proteins are broken down to form urea, carbon dioxide, water, and energy. If a large excess is present, they may be converted into glucose and stored as glycogen or fat. In the process of catabolism, amino acids undergo *deamination*. Deamination is

a reaction in which the amino group of an amino acid is split off, forming ammonia and a keto acid. The keto acid is then further oxidized to form carbon dioxide, water, and energy. This process may be illustrated using the simple amino acid, alanine.



These reactions probably occur in several steps, but for simplicity are illustrated in this manner. The end products of these reactions are combined to form urea. Urea formation takes place in the liver by a complicated series of reactions. A simple representation of this process is shown as follows:



Urea is carried by the blood stream to the kidneys where it is excreted in the urine. Urea is the main end product of protein catabolism and accounts for 80 to 90 per cent of the nitrogen that is excreted in the urine.

NITROGEN BALANCE

Since proteins are not stored in the body, an adult whose weight remains constant should excrete the same amount of nitrogen as is contained in his food. Any repair of tissues would merely represent an exchange of amino acids without appre-

ciably affecting the intake or excretion of nitrogen. A person who excretes an amount of nitrogen in the urine, feces, and perspiration equal to that taken in as food is said to be in *nitrogen balance*.

A growing child will retain considerable quantities of nitrogen in the protein of newly formed body tissue. He will therefore excrete less nitrogen than is present in his diet; he is said to have a *positive nitrogen balance*. Any condition which results in the formation of new tissues in the body, such as recovery from a wasting illness or an extensive program of muscular development, will be characterized by a positive nitrogen balance.

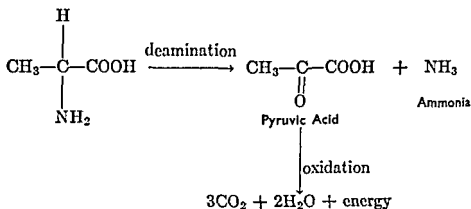
When the nitrogen excretion is greater than the intake of nitrogen, the body is said to have a *negative nitrogen balance*. Starvation, prolonged fevers, malnutrition, and any wasting disease will produce a negative nitrogen balance. If a person continues on a negative nitrogen balance, the body tissues will eventually exhaust the protein available for energy production, and death will occur. Large amounts of sugar are often given to patients suffering from prolonged fevers to spare the protein tissue as much as possible.

PROTEIN MINIMUM

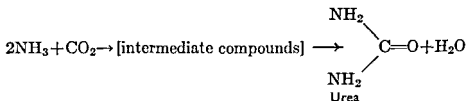
Many investigators have attempted to determine the minimum amount of protein a person can eat and still maintain a nitrogen balance. From his extensive work in this field, Hinshelwood suggested that nitrogen balance could be maintained on an intake of 30 to 40 gm. of protein per day. If the protein of the diet contained the proper assortment of amino acids, as low as 15 gm. per day was sufficient. Modern nutritional workers recommend a daily intake of at least 60 gm. of protein to insure an adequate supply of the different amino acids required by the body. The average diet of today supplies 50 to 75 gm. of protein as compared to the higher protein intake (75-100 gm.) of a few years ago.

In order to synthesize such essential substances as tissue proteins, hormones, enzymes, bile salts, and hemoglobin, the body must have a complete assortment of amino acids. These amino

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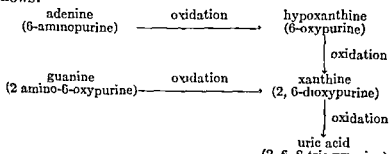
and methionine is converted into sulfates. This sulfur is known as *oxidized sulfur* and may be excreted in the form of *inorganic sulfates* or *etheral sulfates* (organic.) A small fraction of the sulfur is excreted without being oxidized and is called *neutral sulfur*. Cystine makes up the majority of the neutral sulfur. If abnormally large amounts of cystine are excreted in the urine, the condition is called *cystinuria*. An increase in the protein intake causes the excretion of more oxidized sulfur but has little effect on the neutral sulfur.

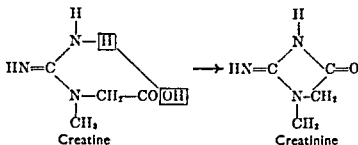
NUCLEOPROTEIN METABOLISM

It has already been stated that nucleoproteins are constituents of nuclear tissue and are composed of a protein conjugated with nucleic acid. During the process of digestion, the protein is broken down to amino acids, and the nucleic acid is hydrolyzed by a series of enzymes to form purines, pyrimidines, phosphoric acid, and sugar. In metabolism, the amino acids and sugar follow the ordinary process of protein and carbohydrate utilization. The phosphoric acid is used to form other phosphorus compounds in the body or may be excreted in the urine as phosphates.

Purine Metabolism

Only the purines and pyrimidines follow a special course in metabolism. *Adenine* (the purine nucleus, with an amino group in position 6, more simply named 6-aminopurine [see p. 140]) and *guanine* (2-amino-6-oxypurine, or an amino group in position 2 and an oxygen connected by a double bond to position 6) are the two purines present in nucleic acid. These purines are deaminized and oxidized through a series of reactions to form *uric acid* (2, 6, 8-trioxypurine). These reactions may be illustrated as follows:





The excretion of creatinine is apparently related to the metabolism of muscles, since it is not affected by the protein intake and the amount excreted is proportional to the quantity of muscle tissue in the body. The milligrams of creatinine excreted per day per kilogram of body weight is called the *creatinine coefficient*. In general, the higher the muscular development, the higher the creatinine coefficient. Men have a creatinine coefficient of about 24, women about 18, and children from 9 to 17. Muscularly underdeveloped or obese men may have a low coefficient (15 to 18), while women who are muscularly developed may have a coefficient as high as 24.

Creatine is normally excreted by children up to the age of puberty. It may also be present in the urine during menstruation and in the latter stages of pregnancy. It is not found in the urine of normal men. The pathological excretion of creatine, called *creatinuria*, occurs in conditions of abnormal carbohydrate metabolism, such as diabetes and starvation. Many diseases of the muscles in which the muscle cells are broken down give rise to the excretion of creatine in the urine. Muscular dystrophy, muscular atrophy, and myasthenia gravis are examples of such diseases.

SULFUR METABOLISM

The sulfur of the body is largely derived from the sulfur-containing amino acids, *cystine* and *methionine*, which are present in the proteins of food. Certain tissue proteins of the body, such as hair and fingernails, are rich in sulfur, containing from 10 to 15 per cent cystine. Taurocholic acid, a bile acid, contains sulfur, as does glutathione and vitamin B₁. The last two compounds are important in biological oxidation-reduction reactions.

When protein is catabolized in the body, the sulfur of cystine

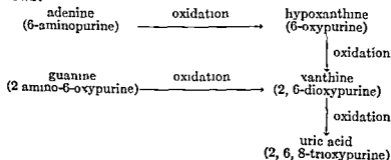
and methionine is converted into sulfates. This sulfur is known as *oxidized sulfur* and may be excreted in the form of *inorganic sulfates* or *ethereal sulfates* (organic). A small fraction of the sulfur is excreted without being oxidized and is called *neutral sulfur*. Cystine makes up the majority of the neutral sulfur. If abnormally large amounts of cystine are excreted in the urine, the condition is called *cystinuria*. An increase in the protein intake causes the excretion of more oxidized sulfur but has little effect on the neutral sulfur.

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Mammals other than man and apes have an enzyme (uricase) which catalyzes the further oxidation of uric acid to *allantoin*. Uric acid, however, is the end product of purine metabolism in man and is excreted in the urine.

Little is known about the metabolism of pyrimidines except that they are probably changed to urea, which is excreted in the urine. There is ample evidence to suggest that both purines and pyrimidines may be synthesized in the body, even when they are not present in the diet. Since these substances are necessary in the formation of cells, this power of synthesis is extremely important. A growing baby lives on milk, which contains no purines, yet he is continually building new cells. A salmon travels miles up rivers to its spawning beds, with nothing to eat, yet *it builds considerable nuclear material on the trip.*

REVIEW QUESTIONS

1. What main processes remove amino acids from the blood stream after a meal rich in protein?
2. Why is the synthesis of protein more important in the metabolism of a child than in that of an adult?
3. How does an adult use the majority of the amino acids that enter the blood stream? Why?
4. What essential difference exists between the end products of catabolism of proteins compared to those from carbohydrates or fats?
5. What condition would exist in the body if the ammonia that is formed from deamination of amino acids was not converted into urea?
6. Would it be possible for a person to be in nitrogen balance at one time, have a positive nitrogen balance at another, and a negative nitrogen balance at still another time? Explain.
7. Why is it inadvisable to feed growing children on a minimum amount of dietary protein?
8. Define the following terms: essential amino acid, complete protein, and incomplete protein.
9. Why are creatine and phosphocreatine important compounds in the body?
10. The creatinine coefficient of an athlete is usually higher than that of a business man. Explain.
11. Name four important sulfur-containing compounds present in the body.
12. What happens to the sulfur of cystine and methionine when these substances undergo catabolism?

13. Why is purine metabolism an important aspect of nucleoprotein metabolism?
14. Outline the steps involved in the formation of uric acid in the body.
15. Plan a simple experiment to prove that purines and pyrimidines are synthesized in the body when they are not present in the diet.

CHAPTER XX

The Blood

THE circulation and transportation of nutrient and waste materials in the body are accomplished by the *blood*, *lymph*, and *tissue fluid*. The blood circulates in a closed system and does not come into direct contact with the tissue cells. The lymph is carried by a system of vessels called the *lymphatics* and is similar in composition to the plasma of the blood and the fluid which surrounds the tissues. The lymph and tissue fluid are often referred to as *interstitial fluid* and constitute about 15 per cent of the body weight. This interstitial fluid plays an important role in the exchange of material between the blood and tissues.

Functions of the Blood

Some idea of the importance of blood to the body may be gained from a consideration of its major functions, which follow:

1. The blood transports nutrient material to the tissues and waste products of metabolism to the organs of excretion.
2. It functions in respiration by carrying oxygen to the tissues and carbon dioxide back to the lungs.
3. It distributes regulatory substances, such as hormones, vitamins, and certain enzymes, to the tissues in which they exert their action.
4. The blood contains white corpuscles, antitoxins, precipitins, and so on, which serve to protect the body against micro-organisms.
5. It plays an important role in the maintenance of a fairly constant body temperature.

GENERAL COMPOSITION

Volume

Blood composes approximately 9 per cent, or one-eleventh to one-twelfth of the body weight. This means that a person weighing 120 pounds would have about 5 liters of blood. The loss of a small quantity of blood in bleeding or the donation of 500 cc. for transfusion or to the Red Cross does not cause adverse effects. The blood volume is rapidly regenerated after such loss, and the missing constituents are replaced in a reasonably short period. The volume of the blood decreases in hemorrhage, diarrhea, and vomiting, and increases in fever and pregnancy.

Formed Elements

The two major portions of blood are the formed elements and the plasma. When separated by centrifugation, the formed elements occupy from 40 to 45 per cent by volume of the blood. This fraction contains the red blood cells, white blood cells, and thrombocytes (platelets).

The red blood cells, or *erythrocytes*, contain the respiratory pigment hemoglobin and have several important functions. The number of red blood cells in men is approximately 5,000,000 per cubic millimeter, in women approximately 4,500,000. The determination of the number of red cells in the blood is often carried out in the laboratory since the value changes markedly in certain diseases. The red cell count is especially important in diagnosis and treatment of anemia, which is characterized by a lowered red cell count and a decrease in hemoglobin.

White blood cells, or *leukocytes*, are larger than red cells and have nuclei which red cells do not. Normally, there are from 5000 to 10,000 white cells per cubic millimeter of blood. There are several types of white blood cells, and they all function to combat infectious bacteria. In several diseases and especially in acute infections, the white cell count increases. Laboratory determinations of the number of white cells is therefore commonly used as diagnostic aids in such conditions as acute appendicitis.

Thrombocytes (platelets) are even smaller than red blood cells and do not contain a nucleus. There are from 250,000 to 400,000

thrombocytes per cubic millimeter in the blood of a normal person. Their major function is in the process of blood clotting, since they contain cephalin, a phospholipid involved in the early stages of clotting.

Serum and Plasma

When freshly drawn blood is allowed to stand, it clots and a pale yellow fluid soon separates from the clotted material. This fluid is called *serum* and is blood minus the formed elements and fibrinogen which is used in the clotting process. If, on the other hand, blood is centrifuged, the fluid portion that separates from the cells is called *plasma*. The plasma contains fibrinogen as well as other important proteins. From 55 to 60 per cent of the blood volume is plasma.

Plasma Proteins

The proteins of the plasma are present in a concentration of about 7 per cent. The most important of these are *albumin*, the *globulins*, and *fibrinogen*. Recently, the globulins have been separated into several fractions of different molecular size and properties by the modern technic of *electrophoresis*, as can be seen in the following table.

PER CENT OF PLASMA PROTEINS	
Albumin	60
Globulins	
alpha ₁ (α_1)	5
alpha ₂ (α_2)	9
beta (β)	11
gamma (γ)	10
Fibrinogen	5

The electrophoretic analysis of the plasma proteins is of great clinical interest since the proportion of the proteins varies considerably in certain diseases. For example, the changes in the protein components of plasma in cirrhosis or in nephrosis are so striking that the analysis may be used in diagnosis.

The plasma proteins have several functions in the body, of which the most essential is the maintenance of the effective

osmotic pressure of the blood which controls the water balance of the body. The interchange of water between blood and tissue spaces depends on the plasma proteins, and a decrease, especially in albumin, will cause water to flow from the blood into the tissues, resulting in a condition of *edema*. The globulins contain the immunologically active antibodies against such diseases as diphtheria, influenza, mumps, and measles. These immune principles are especially concentrated in the *gamma globulin* fraction. *Fibrinogen* is an essential component in the blood clotting process. During the war, methods of separating the proteins of the plasma were devised and the clinical use of these fractions is being studied. Two of the separated proteins, human serum albumin and gamma globulin, have already undergone considerable clinical trial. The concentrated serum albumin has been used in cases of shock, cirrhosis, nephrosis, extensive hemorrhage, and in edema, while gamma globulin has been used in the prevention and treatment of measles. Another fraction, fibrinogen, which is relatively easy to separate from the other plasma proteins, has been employed in the production of *fibrin films*, *fibrinogen plastics*, and *fibrin foam*. The films have been fabricated into sheets, threads, and tubes for use in surgery, whereas the foam finds extensive use as a hemostatic agent in surgery and neurosurgery. Severely burned areas of the skin have been protected by precipitating a fibrin film over the surface of the burn.

Blood Clotting

There have been many theories proposed to explain the complex mechanisms of the clotting of blood. Perhaps the most commonly accepted is the modern version of Howell's original theory, a rough approximation of which is shown in outline form (p. 232). The thrombocytes and tissue cells contain a *thromboplastic factor* (probably a cephalin-protein complex) which effectively neutralizes the action of *antiprothrombin*, which normally prevents *prothrombin* from being converted into *thrombin*. The prothrombin released by this action reacts with Ca^{++} present in the blood to form thrombin. The thrombin acts as an enzyme to convert the

Blood is shed—disrupting thrombocytes and injured tissue cells

↓
thromboplastic factor (cephalin)

which combines with

antiprothrombin to free

↓
prothrombin

which in the presence of

Ca^{++}

↓
thrombin

which converts

fibrinogen

into

↓
fibrin (the clot)

fibrinogen of the plasma into *fibrin*, which is the clot. A common antiprothrombin is *heparin*, a glucuronic acid-sulfate complex which is formed in the liver and circulates in the blood.

Blood drawn from a normal person usually clots within five minutes. The *clotting time* of blood flowing from an injury varies from about two to six minutes. In the disease known as *hemophilia*, the clotting time may be prolonged to forty or fifty minutes. This is obviously a serious situation, since a nosebleed, tooth extraction, or minor injury may threaten the life of a hemophilic person. The disease is hereditary, occurring only in males, although it is transmitted by females. All of the blood-clotting factors are present in normal amounts in hemophilia, but the thrombocytes are more resistant to disruption than those in normal blood. Also the conversion of prothrombin to thrombin is abnormally slow, suggesting a deficiency in the thromboplastic mechanism.

As can be seen from the outline of the clotting process, blood

should not clot in the blood vessels. Nevertheless, intravascular clotting occurs occasionally, and such a clot is called a *thrombus*. For example, after an operation or injury to blood vessels or tissue, a local concentration of thromboplastin might occur, causing a clot within the vessel. If the thrombus clings to the blood vessel, it is gradually absorbed with no serious consequences. If, however, the thrombus breaks loose and is carried by the blood stream, it becomes an *embolus* and may cause paralysis or death if it obstructs certain vessels in the brain or heart. The intravenous injection of heparin to prevent *thrombosis* after certain types of surgery has been tried recently with promising results.

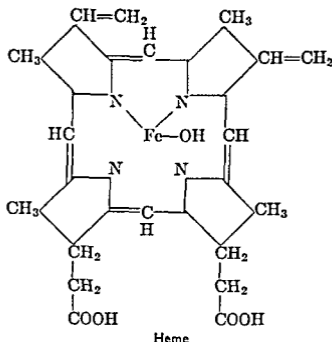
Anticoagulants

The simplest way to prevent drawn blood from clotting is to remove the calcium ions or repress their ionization. An oxalate removes the calcium by precipitation, whereas a citrate represses the ionization of calcium ions. When blood is drawn for analysis, oxalates are almost always used as the *anticoagulant*. Blood for transfusion is protected from clotting by citrates, since oxalates are poisonous. Heparin is sometimes used as an anticoagulant since it acts as an antiprothrombin substance and prevents the formation of prothrombin. Blood-sucking leeches secrete a substance called *hirudin*, which acts as an antithrombin and prevents the conversion of fibrinogen to fibrin.

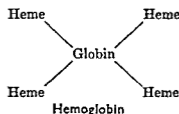
Hemoglobin

Hemoglobin is a conjugated protein composed of the pigment *heme* and the protein *globin*, which is a histone. Heme is a complex molecule containing iron, four pyrrole groups, and hydrocarbon chains as shown on page 234.

It has been determined that four heme molecules combine with one globin to form hemoglobin with a molecular weight of approximately 68,000. The point of attachment of the heme and



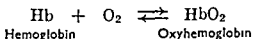
globin is not certain, but the hemoglobin molecule may be represented as follows:



The normal concentration of hemoglobin in the blood varies from 14 to 16 gm. per 100 cc. This means that a 120-pound person would have a total of approximately 750 gm. of hemoglobin. Since the red blood cells which contain the pigment are constantly being broken down, there is a continuous degradation of hemoglobin into other pigments in the body, for example, *bilirubin* which is converted into pigments responsible for the characteristic color of bile, urine, and feces.

Hemoglobin is often called the *respiratory pigment* of the blood and has the property of combining with gases to form

various derivatives. Most important of these is *oxyhemoglobin*, a combination of oxygen and hemoglobin.



It can be seen from the equation that the reaction is reversible, a very important consideration in respiration since hemoglobin combines with oxygen in the lungs and carries it to the tissues where it gives up its oxygen to form hemoglobin again. Another derivative of oxygen and hemoglobin is *methemoglobin*, which is more stable than oxyhemoglobin, containing only one-half the oxygen in a form that is not readily given up to the tissues. Methemoglobin can be represented as HbO and is produced in the body by the action of certain drugs and poisons such as antipyrine, iodine, sulfa drugs, and nitrobenzene. Since it does not act as a respiratory pigment, its production in excessive amounts would cause respiratory difficulties.

Carbon monoxide hemoglobin, HbCO, sometimes called carboxy hemoglobin, is a combination of the colorless, odorless gas and hemoglobin. Since the affinity for *carbon monoxide* is over 200 times that for oxygen, hemoglobin will combine with small concentrations of carbon monoxide and accumulate in the blood. The compound is more stable than oxyhemoglobin, and if sufficiently large amounts are formed, death will occur from respiratory failure. Carbon monoxide is found in the gaseous products of combustion, as in automobile exhaust gas, furnace gases, and in illuminating gas. To illustrate the danger of breathing carbon monoxide gas, death may occur in five to ten minutes if illuminating gas is escaping in a small closed kitchen or if an automobile motor is kept running in a one-car garage without ventilation.

Anemia

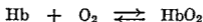
There are many types of anemia, but they are all characterized by a decrease in the red cell count or in the concentration of hemoglobin. Primary, or *pernicious anemia*, is caused by a deficiency of the red blood cell producing mechanism in the bone marrow. In this disease, the erythrocytes are formed more slowly

than they are destroyed, with a resultant decrease in red cell count and hemoglobin concentration. Considerable research has been directed at the problem of pernicious anemia and has resulted in a more satisfactory treatment of this disease. At present, pernicious anemia can be controlled by the ingestion of liver and stomach extract and the vitamin, folic acid.

Secondary anemia is caused by more indirect factors, such as loss of blood by hemorrhage, cancer, certain infections, and intestinal parasites. This type of anemia is readily cured by removing the cause. *Nutritional anemia* usually results from the lack of iron in the diet and may appear in severe malnutrition or protein deprivation. A diet containing adequate quantities of iron, proteins, and vitamins is used to treat nutritional anemia.

Respiration

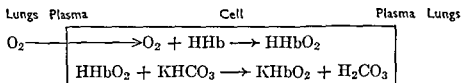
By far, the most important function of hemoglobin is in respiration, to help carry *oxygen* from the lungs to the tissues and *carbon dioxide* from the tissues to the lungs. The transportation of oxygen by the blood depends on the reversible reaction between hemoglobin and oxygen.



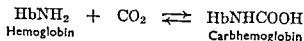
The oxygen capacity of the blood, about 1000 cc., is sufficient for normal tissue requirements. Some conception of the role of hemoglobin may be gained by a comparison of the oxygen capacity of plasma and whole blood. One liter of plasma can carry only 3 cc. of oxygen in solution. In the absence of hemoglobin, our circulatory system would have to contain over 300 liters of fluid to supply oxygen to the tissues. This would represent a system four to five times our body weight.

In the process of respiration, hemoglobin comes into contact with a relatively rich oxygen atmosphere in the alveoli of the lungs to form oxyhemoglobin. The oxyhemoglobin is carried by the arterial circulation to the tissues where a low oxygen concentration and high carbon dioxide concentration combine to release the oxygen to the tissues. The carbon dioxide is then carried back to the lungs for excretion and the cycle is repeated.

The complete detailed mechanism of respiration is very complicated; however, in view of its importance, the essential points will be outlined. Oxygen from the air is breathed into the alveoli of the lungs. Because of the difference in oxygen pressure in the alveoli and capillaries and because of the affinity of hemoglobin for oxygen, the gas passes into the red blood cells and combines with hemoglobin to form oxyhemoglobin. Before leaving the capillaries of the lungs, the oxyhemoglobin, which is an acid compound (represented as HHbO_2), reacts with bicarbonates to form carbonic acid and a basic form of oxyhemoglobin (represented as KHbO_2).



The oxyhemoglobin is then carried to the tissues where carbon dioxide is being formed as a result of tissue metabolism. The carbon dioxide diffuses into the red blood cell where the enzyme *carbonic anhydrase* catalyzes its combination with water to form carbonic acid. Because of the difference in oxygen pressure between the capillaries and the tissues, the oxyhemoglobin breaks into oxygen and hemoglobin and the gas diffuses into the tissues to be used in the oxidative reactions of metabolism. As the carbon dioxide continues to diffuse into the red cell from the tissues, it first forms more carbonic acid and then the carbonic acid is neutralized by the basic hemoglobin to form bicarbonates. As the bicarbonate concentration increases, it diffuses out of the cell into the plasma. The loss of negative ions from the cell is then balanced by a migration of chloride ions into the cell from the plasma to establish ionic or electrolyte equilibrium. This process is known as the *chloride shift*. In addition, some of the carbon dioxide that diffuses into the cell combines with hemoglobin to form *carbhemoglobin* as shown in the following reaction.

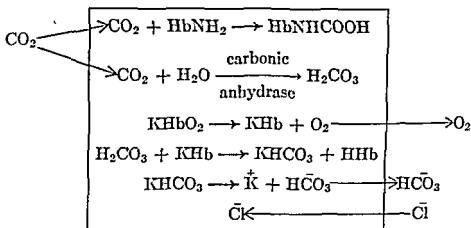


Thus the carbon dioxide, partly as carbonic acid, partly as carbohemoglobin, and the rest as bicarbonates in the cells and plasma, is carried back to the lungs.

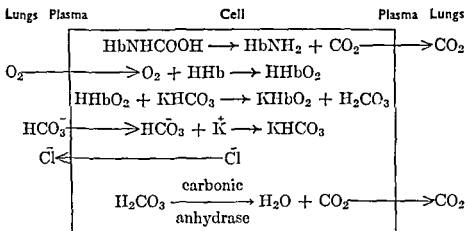
Tissue Plasma

Cell

Plasma Tissue

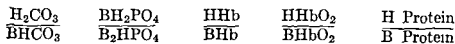


In the lungs, the carbohemoglobin releases its carbon dioxide which diffuses into the alveoli for excretion. The freed hemoglobin along with other hemoglobin that had given up its oxygen in the tissues then combines with oxygen from the alveoli as described previously. The oxyhemoglobin that is formed is an acid substance and reacts with bicarbonates to form carbonic acid. The carbonic acid is rapidly converted into carbon dioxide and water by the reversible enzyme, *carbonic anhydrase*. This carbon dioxide also diffuses into the alveoli for excretion. In addition to these reactions, the bicarbonate in the plasma diffuses into the cell to replace the bicarbonate that was converted into carbon dioxide, thus forming more of the gas for excretion by the reactions just discussed. To balance the loss of negative ions from the plasma, the chloride ions diffuse out of the cell into the plasma causing a chloride shift opposite in direction to that in the tissues. The carbon dioxide is thus carried to the lungs and excreted and the respiratory cycle is ready to be repeated.

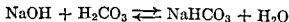


Acid-Base Balance

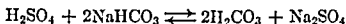
The *pH* of the blood is maintained slightly on the alkaline side of neutrality between 7.35 and 7.45. Since a change to a more acid or alkaline *pH* causes serious disturbances in the *acid-base balance* of the body, several factors combine to maintain the *pH* of the blood within these narrow limits. Most important of these are the buffer systems in the plasma and cells. *Buffers* are combinations of weak acids and their salts which are able to withstand additions of acid or alkali without appreciable change in *pH*. The following buffers operate to maintain the reaction of the blood. (H represents the acid salt and B the basic salt of a compound):



To illustrate buffer action, let us assume that an excess of a strong base, NaOH, enters the blood. Using the important *carbonic acid-bicarbonate buffer*, the reaction would be as follows:



The strong base would therefore be neutralized by being converted into a salt of a weak acid which in itself is part of the buffer system. If excessive quantities of NaHCO_3 were formed, it would be excreted by the kidney. Conversely the presence of



The strong acid would be converted into a weak acid which is also part of the buffer system and is excreted as carbon dioxide in the lungs as described in the foregoing section on respiration. The ability of the combined buffer systems of the blood to neutralize acid is expressed as the *alkali reserve* of the blood. If an excess of acid causes the *pH* of the blood to drop below 7.35, a condition of *acidosis* exists; and the alkali reserve would be lower than normal. On the other hand, the opposite condition of *alkalosis* where the *pH* of the blood rises above 7.45 would result in an increase in alkali reserve.

The *phosphate buffer* is composed of a mixture of an acid salt, NaH_2PO_4 , and a basic salt, Na_2HPO_4 . These salts buffer acid or alkali in a similar fashion to the carbonic acid and bicarbonate system. Any excess of acid or basic phosphate salt formed in the blood is rapidly excreted by the kidney. In fact, the *pH* of the urine is closely related to the phosphate buffer system of the blood since many of the acids or alkaline products of metabolism are excreted as phosphate salts.

The acid-base balance of the body is also aided by the ability of the kidney to produce ammonia. This ammonia combines with acid products of protein metabolism forming ammonium salts which are excreted by the kidney enabling the body to save the sodium and potassium for the blood buffer systems. On a high protein diet or in conditions of acidosis, the ammonia excretion increases thus illustrating another mechanism that operates to maintain the constancy of the *pH* of the blood.

Changes in the Composition of the Blood

The major components of the blood have already been discussed, as well as some of the changes that occur in disease. *Blood analysis* is extremely important in clinical medicine, and laboratory findings are often used in diagnosis. A multitude of methods have been devised for the determination of the various constituents with emphasis on simplicity, speed, and the use of small samples of blood. The following table presents a compari-

CONSTITUENT	NORMAL RANGE	PATHOLOGICAL CONDITIONS IN WHICH INCREASES OCCUR (UNLESS OTHERWISE INDICATED)
	Per Cent	
Total solids	19-23	Anhydremia. Low in hydremic plethora and anemia.
Total proteins (serum)	6.5-8.2	Anhydremia. Low in nephritis with edema (nephrosis).
Albumin (serum)	4.6-6.7	Low in nephrosis.
Globulin (serum)	1.2-2.3	Nephrosis, anaphylactic conditions, malignancy, infections, muscular activity.
Fibrinogen (plasma)	0.3-0.6	Pneumonia, infections. Low in cirrhosis of liver, chloroform or phosphorus poisoning, typhoid fever
Hemoglobin	14-16	Polycythemia. Low in primary and secondary anemia, chlorosis.
Total nitrogen	3.0-3.7	Varies chiefly with proteins (albumin, globulin, hemoglobin).
	mg. per 100 cc.	
Nonprotein nitrogen	25-35	Nephritis, eclampsia, etc. See Urea N.
Urea Nitrogen	10-15	Chronic and acute nephritis, metallic poisoning, cardiac failure, intestinal or prostatic obstruction, some infectious diseases. Relatively low in nephrosis.
Amino acid nitrogen	5-8	Leukemia, acute yellow atrophy of the liver, severe nephritis.
Uric acid	2.0-3.5	Nephritis, gout, arthritis, eclampsia.
Creatinine	1-2	Nephritis.
Creatine	3-7	Terminal nephritis.
Ammonia nitrogen	0.1-0.2	Terminal interstitial nephritis.
Undetermined nitrogen	4-18	Eclampsia.

(After Hawk, Oser, and Summerson: Practical Physiological Chemistry. Philadelphia, The Blakiston Co.)

CONSTITUENT	NORMAL RANGE	PATHOLOGICAL CONDITIONS IN WHICH INCREASES OCCUR (UNLESS OTHERWISE INDICATED)
	mg. per 100 cc.	
Glucose	70-100	Diabetes, pregnancy, severe nephritis.
Total acetone bodies	0.8-5.0	Diabetes.
Total fatty acids	290-420	Diabetes, nephritis.
Cholesterol	150-190	Diabetes, nephritis, nephrosis, biliary obstruction, pregnancy. Low in pernicious anemia.
Lipid phosphorus	12-14	Diabetes, nephritis, pregnancy. In anemia, low in plasma, high in cells.
Bilirubin	0.1-0.25	Biliary obstruction, hemolytic anemias. Low in secondary anemia.
Chlorides, as NaCl	450-500	Nephritis, cardiac conditions, prostatic obstruction, eclampsia, anemia. Low in diabetes, fever, and pneumonia.
Sulfates as S (serum)	0.9-1.1	Nephritis.
Phosphorus as P (plasma)	3-4	Nephritis. Low in rickets. Normal values 1-2 mg. higher in children.
Calcium (serum)	9.0-11.5	Low in infantile tetany, severe nephritis, parathyroidectomy.
Magnesium (serum)	1-3	No changes noted in disease.
Sodium (serum)	330	Low in cases of alkali deficit.
Potassium (serum)	16-22	Pneumonia, acute infections, occasionally in uremia.
	vol. per cent	
CO ₂ capacity (plasma)	55-75	Respiratory diseases, tetany. Low in diabetes, nephritis.
O ₂ capacity	16-24	Polycythemia, anhydremia. Low in cardiac and respiratory diseases, anemia.

son of some of the blood constituents in normal and abnormal conditions. It can readily be seen that important variations occur in several diseases.

REVIEW QUESTIONS

1. Outline the major functions of the blood.
2. What are the formed elements of the blood? Why are they important?
3. What is the difference between serum and plasma?
4. Briefly discuss the plasma proteins and their functions in the body.
5. Outline a process for the clotting of blood.
6. What is hemophilia and what relation does it have to the clotting of blood?
7. How would you prevent a sample of blood from clotting? Name three anticoagulants.
8. Approximately how much hemoglobin is present in 100 cc. of blood?
What is the composition of the hemoglobin molecule?
9. Why is it dangerous to breathe carbon monoxide gas?
10. Briefly discuss three types of anemia, their cause, and treatment.
11. Write an equation for the reaction of hemoglobin and oxygen gas.
Why is the reversibility of this reaction important?
12. What is carbonic anhydrase and what is its function in the blood?
13. In respiration, what happens to the oxygen that is taken in the lungs?
14. How is the carbon dioxide that is released in the tissues carried to the lungs?
15. What are buffers? How do they help maintain the acid-base balance of the body?
16. Explain the terms: alkali reserve, acidosis, and alkalosis.
17. In what way does the production of ammonia by the kidney help maintain the acid-base balance of the body?

CHAPTER XXI

The Urine

THE end products of metabolism are excreted mainly through the lungs and the kidneys. The lungs eliminate water and carbon dioxide and may aid in the removal of other volatile substances. The kidney, the most important organ of excretion, eliminates water, inorganic salts, and the end products of metabolism. This organ plays an important part in the maintenance of the composition of the blood, the pH of the blood and tissues, and the osmotic pressure relations of the blood and tissue fluids.

Waste products of metabolism may also be removed from the body through the skin, the liver, and the intestines. The skin eliminates small amounts of water, inorganic salts, nitrogenous material, and lipids. Cholesterol, bile pigments, and bile salts are excreted by the liver, whereas inorganic salts are eliminated by the intestines.

The end products of protein metabolism are found mainly in the urine. Quantitative analysis of these nitrogen-containing constituents gives valuable information about the dietary habits of an individual.

THE FORMATION OF URINE

The kidney may be regarded as a filter through which the waste products of metabolism are passed to remove them from the blood. The blood enters the kidney by means of the renal arteries, which break up into smaller branches leading to the small filtration units called *Malpighian corpuscles*. Each human kidney contains approximately 4,000,000 to 5,000,000 of these units. A Malpighian corpuscle consists of a mass of capillaries

from the renal artery which form the *glomerulus*. The glomerulus is enclosed within a capsule called *Bowman's capsule* which opens into a long tubule. Several of these tubules are connected to larger *collecting tubules* which carry the urine to the bladder.

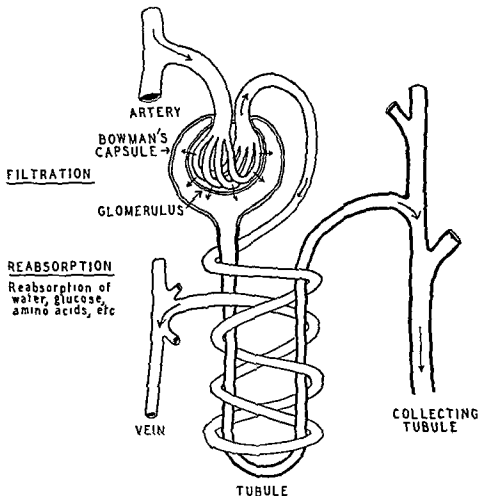


Fig. 47. A filtration unit of the kidney.

These anatomical structures of the kidney are illustrated in Fig. 47.

The most generally accepted theory for the formation of urine may be outlined as follows: As the blood passes through the glomerulus, the constituents other than protein filter through

the capillary walls and enter the tubules. As this filtrate passes down the tubules, a large proportion of the water and any substances which are of value to the body, such as glucose, certain inorganic salts, and amino acids, are reabsorbed into the blood stream. These substances are called *threshold substances*. Waste products of metabolism such as urea, uric acid, and creatinine are not reabsorbed and therefore appear in the urine. It has been estimated that 67 liters of plasma filter through the glomeruli every day to form approximately 1 liter of urine. The other 66 liters are therefore reabsorbed from the tubules to reenter the blood stream. The importance of the reabsorption mechanism cannot be overestimated, because death would result from dehydration if this process failed to function.

THE COLLECTION OF URINE

An accurate estimation of the quantity of a substance excreted in a day or a qualitative test for its presence in the urine is best carried out on a *twenty-four-hour specimen* of urine. This is due to the variation in urinary excretion at different times during the day, and the fact that some pathological constituents may be excreted only at certain periods of the day. A twenty-four-hour specimen is usually collected by discarding the urine from the first voiding of the morning, and saving all the urine that is passed during the day up to and including the first voiding of the following morning. The specimen is usually preserved by covering it with a thin layer of toluene. When the urine cannot be analyzed at once, it should be kept in a stoppered bottle in a cold place.

GENERAL PROPERTIES OF URINE

Volume

A normal adult will excrete from 800 to 1600 cc. of urine in twenty-four hours. The volume is obviously influenced by the amount of liquids consumed and is decreased in hot weather or by severe muscular exercise. Men as a rule excrete more urine (1200–1600 cc. per day) than women do (800–1200 cc.).

The volume of urine may be decreased below normal in conditions like fevers and diarrhea where excessive amounts of

water are lost by other channels of excretion. This decrease in the urinary output is called *oliguria*; a total lack of urinary excretion is known as *anuria*, which is frequently associated with extensive kidney damage. Anuria may be caused by transfusion with the wrong type of blood or by poisoning with salts of heavy metals.

The urine volume may be increased to above normal, a condition known as *polyuria*, by the excessive intake of fluids, and may also be caused by certain diseases. Patients with diabetes mellitus and with nervous disorders show a fairly marked polyuria; however, *diabetes insipidus* is accompanied by an extreme polyuria with volumes ranging from 20 to 50 liters per day. Any substance that causes polyuria is called a *diuretic*. Caffeine is a good example of a diuretic that is widely used in medicine. The end products of protein metabolism, especially urea, are diuretics, which accounts for the increase in the volume of urine excreted by patients on high protein diets

Color

Normal urine is yellow in color but may vary from a straw to a deep amber color. The chief pigment of normal urine is *urochrome*, a mixture of urobilinogen and urobilin. The amount of urochrome excreted per day is fairly constant, therefore the color of the urine is directly proportional to the volume. A twenty-four-hour specimen with a large volume has a light straw color compared to the brown color of a specimen with a low volume.

The color of the urine is often altered by the presence of abnormal constituents. Hemoglobin causes a brown to a red color when present in the urine. In cases of jaundice, the bile pigments that are excreted in the urine color it a greenish-brown. Brown or black urine may be due to the presence of phenols from carbolic acid poisoning.

Freshly voided urine is usually transparent; it may be turbid after a heavy meal due to the precipitation of calcium phosphate. Infections of the urinary tract are characterized by turbid urines due to the large increase in the number of pus cells present. When

urine specimens are allowed to stand, the urine becomes alkaline and phosphates may precipitate.

Reaction

Normal urine is usually slightly acid in reaction, with a pH of 6. The acidity of urine is due to acid phosphates, sulfates, and organic acids. Protein foods increase the acidity of the urine

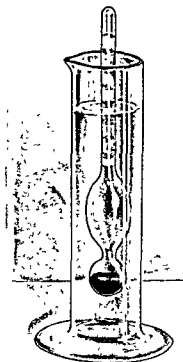


Fig. 48. A urinometer. This apparatus is used to determine the specific gravity of a urine specimen. (Courtesy of Sharp and Dohme, Philadelphia.)

because of the increased formation of phosphates and sulfates. The acidity is also increased in diabetes and in starvation, owing to the increased excretion of acetone bodies. Vegetables and fruits usually produce an alkaline urine because of the alkaline ash they form when they are oxidized in the body. The urine is often alkaline following a heavy meal. The formation of hydrochloric acid in the gastric juice is accompanied by an increase

in the blood concentration of alkaline salts which are excreted in the urine. This temporary alkalinity of the urine is called *alkaline tide*.

Specific Gravity

The specific gravity of urine depends on its concentration of solid waste products. The lower the volume, the greater the concentration and the higher the specific gravity. The specific gravity of normal urine ranges from 1.008 to 1.030 (grams per cubic centimeter) with an average of about 1.018. The total solids in a liter of urine may be approximated by multiplying the second and third decimal figures of the specific gravity by 2.6 (Long's coefficient). For example, a specimen of urine with a specific gravity of 1.020 would have approximately 52 gm. (20 x 2.6) of solids per liter.

NORMAL CONSTITUENTS OF THE URINE

Most of the normal constituents of the urine are affected by the diet and therefore change in amount from day to day. The average quantity of several important constituents excreted in twenty-four hours is given in the following table:

CONSTITUENT	GRAMS IN TWENTY-FOUR HOURS
Water.	1200
Total solids.	60
Urea.	30
Uric acid.	0.6
Creatinine.	1.4
Chlorides as NaCl.	12.0
Phosphates as P_2O_5	1.8
Total sulfur as SO_4	2.5
Ammonia.	0.7

Organic Constituents

Urea. The principal nitrogen-containing constituent of the urine is urea, which accounts for 80 to 90 per cent of the total nitrogen excretion. The amount of urea excreted depends on the protein in the diet; a high protein intake increases, while a low protein intake decreases the urea output. The urea excretion is

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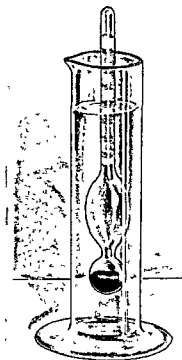


Fig. 48. A urinometer. This apparatus is used to determine the specific gravity of a urine specimen. (Courtesy of Sharp and Dohme, Philadelphia.)

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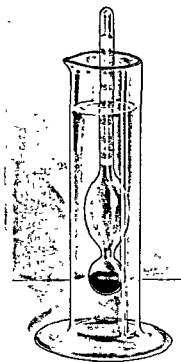


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roteins in the body will cause an increased urinary excretion of uric acid.

The uric acid excretion in man may be increased in conditions where excessive breakdown of nuclear tissue is occurring, as in leukemia and in recovery from pneumonia. The excretion may be decreased in nephritis, uremia, and gout. Gout is characterized by an increase of uric acid in the blood and by the deposition of uric acid or urates in the joints and tissues (Fig. 49). This painful condition was more frequent a few decades ago when larger quantities of meat were consumed.

Creatinine. The urinary excretion of creatinine, the anhydride of creatine, is relatively independent of the protein intake. From 1 to 1.7 gm. of creatinine are excreted per day; the amount is directly proportional to the muscular development of a person. The creatinine of the urine is thought to have its main origin in the creatine of the muscle. Since the daily urinary creatinine is rather constant in a person, other sources of creatinine must be relatively unimportant.

The creatinine excretion is decreased in fevers, diabetes, and during starvation. In diseases of the kidney that result in extensive breakdown of kidney cells, the uremia that develops is characterized by an increase in the amount of creatinine in the blood.

Inorganic Constituents

Chlorides. Of all the constituents of the urine, chlorides are second only to urea in the amount excreted. There are many inorganic salts in the urine, including the chlorides, phosphates, sulfates, and carbonates of sodium, potassium, ammonium, magnesium, and calcium. Of these, sodium chloride is the most abundant, with 10 to 15 gm excreted in twenty-four hours. The average mixed diet does not contain sufficient sodium chloride to support life, so salt must be added in the preparation of food. Herbivorous animals are particularly dependent on a supply of salt outside of their diet. Wild animals travel miles to salt licks and will chew the handles of woodsman's tools to obtain the salt from the perspiration that soaks into the wood.

decreased in diseases of the liver and acidosis. It may be increased in fevers and diabetes (controlled with insulin).

Urea is usually determined by treating it with *urease*, an enzyme that breaks it down into ammonia and carbon dioxide. The ammonia that is formed is estimated by titration with a standard acid and the urea is calculated from this value. Approximately 30 gm. of urea are excreted per day on a mixed diet.

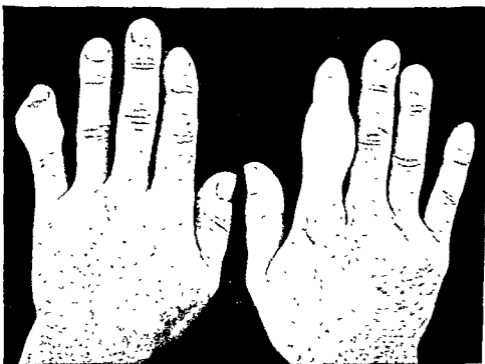


Fig. 49. Deposition of urates (tophi) in the joints of the fingers in gout. (From Duncan, G. G : Diseases of Metabolism. Philadelphia, W. B. Saunders Company.)

Uric Acid. Uric acid is the end product of purine metabolism in man and is excreted as urates (salts of uric acid) in the urine. The daily excretion of uric acid amounts to about 0.6 gm. If the urine is strongly acidified, the urates will be converted to the very insoluble uric acid, which crystallizes out as red pigmented crystals. An increase in the nucleoproteins of the diet (such foods as liver, sweetbreads, and heart) or in the breakdown of nucleo-

ndole and skatole are formed. Small amounts of these substances are absorbed into the blood stream and are detoxified in the liver. In this process, indole forms indoxyl potassium sulfate, which is known as *indican*. Indican is an ethereal sulfate that is excreted in the urine and an increase in its excretion is an indication of abnormal putrefaction in the large intestine.

The neutral sulfur fraction consists mainly of incompletely oxidized sulfur compounds such as cystine, taurine, and sulfides. This fraction is not greatly affected by variation in the diet. In rare cases, large amounts of cystine may be excreted in the urine, a condition known as *cystinuria*.

Ammonia. Approximately 0.7 gm. of ammonia is excreted in twenty-four hours. It is usually in combination with acids such as hydrochloric, sulfuric, and phosphoric. An increase in the excretion of urinary ammonia is caused by acid-forming foods such as meat and cereals, while it is decreased by base-forming foods like fruits and vegetables. The acidosis resulting from the increased production of acetone bodies in diabetes is accompanied by an increased excretion of ammonia. The acetoacetic and β -hydroxybutyric acids are neutralized by ammonia in the kidney before excretion, thus increasing the ammonia in the urine.

The kidney, therefore, has another valuable mechanism for the regulation of the acid-base balance of the body. When large amounts of acid products have to be excreted, the kidney forms ammonia from the urea of the blood to neutralize them. This protects the body from the loss of excessive amounts of sodium and potassium that are needed in the buffers of the blood.

PATHOLOGICAL CONSTITUENTS OF THE URINE

Glucose

Normally the quantity of glucose in the urine is so small that it will not give a positive Benedict test. Various conditions that cause glycosuria have already been outlined in the discussion of carbohydrate metabolism. Since routine examinations of urine always include a Benedict test, it may be well to emphasize the conditions that cause glycosuria. In addition to diabetes mel-

The excretion of sodium chloride in the urine is decreased in fevers and severe muscular exercise. In certain types of nephritis, the concentration of sodium chloride in the blood and tissues causes more water to accumulate, and a condition of edema results.

Phosphates. The urinary excretion of phosphates amounts to about 1.8 gm. in twenty-four hours. Several types of phosphates are present in the urine. The sodium, potassium, and ammonium salts are called *alkaline phosphates*; the calcium and magnesium salts, *earthy phosphates*, and those in organic combination are known as *organic phosphates*. Alkaline phosphates are the most abundant and make up two-thirds of the total urinary phosphates.

The acidity of freshly voided urine is mainly due to the concentration of NaH_2PO_4 . The basic salt, Na_2HPO_4 , predominates in the blood, but the acid salt is present to a greater extent in the urine. The ratio between these two salts is important in the regulation of the pH of the blood and tissue fluids. The acid salt is formed if acid products in the blood are to be excreted by the kidney, whereas an excess of alkaline substances in the blood would result in the excretion of the basic salt.

The amount of phosphates excreted in the urine varies directly with the quantity of phosphorus-containing foods such as casein, nucleoprotein, and phospholipids in the diet. In diseases of the bone (rickets, osteomalacia) the phosphorus excretion is increased, whereas in conditions where bone is being formed (skeletal growth, pregnancy) the excretion is decreased.

Sulfates. As explained under protein metabolism, the end products of sulfur metabolism exist in three forms, *inorganic sulfates*, *ethereal sulfates*, and *unoxidized or neutral sulfur*. These products are excreted in the urine, the daily excretion of total sulfur, expressed as SO_4 , averaging about 2.5 gm. Over three-fourths of the total sulfur is excreted in the form of inorganic sulfates. The sulfur in the urine originates from the sulfur-containing amino acids in the dietary proteins and therefore the quantity excreted is influenced by the nature of the diet. |

During putrefaction of protein material in the large intestine,

ndole and skatole are formed. Small amounts of these substances are absorbed into the blood stream and are detoxified in the liver. In this process, indole forms indoxyl potassium sulfate, which is known as *indican*. Indican is an ethereal sulfate that is excreted in the urine and an increase in its excretion is an indication of abnormal putrefaction in the large intestine.

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litus, the most common causes for a positive Benedict test on the urine are alimentary glycosuria, renal diabetes, and emotional glycosuria. If a urine specimen is collected by the patient several hours after a meal, the alimentary and emotional glycosuria and renal diabetes could be ruled out. If large amounts of glucose are present in the urine at this time, diabetes mellitus is strongly suspected.

A positive Benedict test may be obtained on the urine from pregnant or nursing women, owing to the presence of lactose in the urine. If the sugar is lactose it may be differentiated from glucose by fermentation with yeast. The glucose would be removed from the urine by fermentation, while any lactose present would not be affected. Therefore, a positive Benedict test after fermentation would indicate the presence of lactose in the urine.

Albumin

Normal urine does not contain appreciable amounts of protein because the kidney prevents the passage of such large molecules through the glomeruli when urine is formed. In cases of kidney disease, or *nephritis*, protein escapes from the blood into the urine and causes an *albuminuria*. This condition is sometimes called *renal albuminuria* to distinguish it from *false albuminuria*, which is due to protein entering the urine below the kidney as it passes through the urinary tract.

In routine examinations, the heat coagulation test is commonly used to determine the presence of protein in the urine. On heating the upper portion of the urine in a test tube, a cloudiness may result which is due to albumin or a precipitate of phosphates. Acidification of the urine with dilute acetic acid will dissolve the phosphate precipitate but not the albumin; therefore, if a precipitate remains after acidification, the urine contains protein.

Acetone Bodies

The acetone bodies (acetoacetic acid, β -hydroxybutyric acid, and acetone) are formed in the liver and oxidized in the muscle

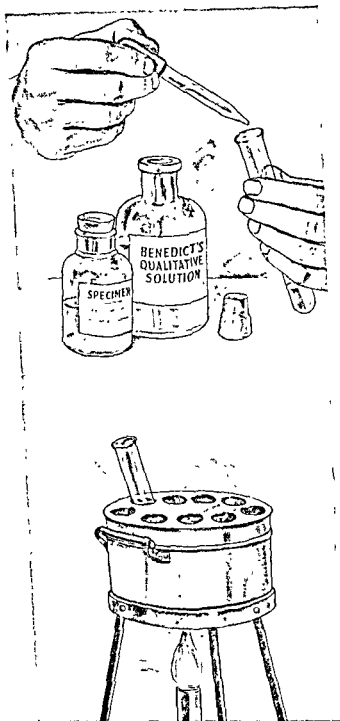


Fig. 50 Technic used in the qualitative test for glucose in the urine.
(Courtesy of Sharp and Dohme, Philadelphia.)

litus, the most common causes for a positive Benedict test on the urine are alimentary glycosuria, renal diabetes, and emotional glycosuria. If a urine specimen is collected by the patient several hours after a meal, the alimentary and emotional glycosuria and renal diabetes could be ruled out. If large amounts of glucose are present in the urine at this time, diabetes mellitus is strongly suspected.

A positive Benedict test may be obtained on the urine from pregnant or nursing women, owing to the presence of lactose in the urine. If the sugar is lactose it may be differentiated from glucose by fermentation with yeast. The glucose would be removed from the urine by fermentation, while any lactose present would not be affected. Therefore, a positive Benedict test after fermentation would indicate the presence of lactose in the urine.

Albumin

Normal urine does not contain appreciable amounts of protein because the kidney prevents the passage of such large molecules through the glomeruli when urine is formed. In cases of kidney disease, or *nephritis*, protein escapes from the blood into the urine and causes an *albuminuria*. This condition is sometimes called *renal albuminuria* to distinguish it from *false albuminuria*, which is due to protein entering the urine below the kidney as it passes through the urinary tract.

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(Courtesy of Sharp and Dohme, Philadelphia.)

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It has already been stated that the kidney has the power to form ammonia from the urea of the blood to combine with these acid compounds, thus sparing the sodium and potassium of the blood buffers. The excretion of acetone bodies is always accompanied by an increase in the output of urinary ammonia. Diabetes mellitus, fevers, prolonged starvation, and the feeding of ketogenic diets are some common causes of acetone body excretion in the urine.

Since the diabetic patient excretes acetone bodies in addition to glucose, a positive Benedict test and a test for acetone bodies is a fairly certain indication of diabetes. All three of the acetone bodies are usually excreted together; therefore, a positive test for one of them is sufficient to prove their presence in the urine. Acetone is most commonly tested for in routine examinations. When a few drops of sodium nitroprusside are added to the urine specimen and the mixture is made alkaline, a wine-red color develops. This color may be caused by acetone or creatinine; however, if the solution is made acid with acetic acid, the color due to creatinine disappears but that due to acetone becomes more intense.

Bile

In cases of *jaundice*, which are usually caused by an obstruction of the bile duct, the blood contains bile. The bile is excreted by the kidney and imparts a greenish brown color to the urine. When the urine is shaken, the foam is colored yellow if bile is present.

Blood

The condition in which blood is present in the urine is called *hematuria* and results from a hemorrhage in the kidneys or in the urinary tract. Any condition which causes hemolysis of red blood cells in the body, such as scurvy, extensive burns, injection of hypotonic solutions, and purpura, is followed by the excretion of hemoglobin and is known as *hemoglobinuria*.

Appreciable amounts of fresh blood in the urine can be detected by the red color that is produced. Smaller quantities

tissue. As discussed previously, in diabetes and in starvation, they accumulate in the blood and are excreted by the kidney. Before

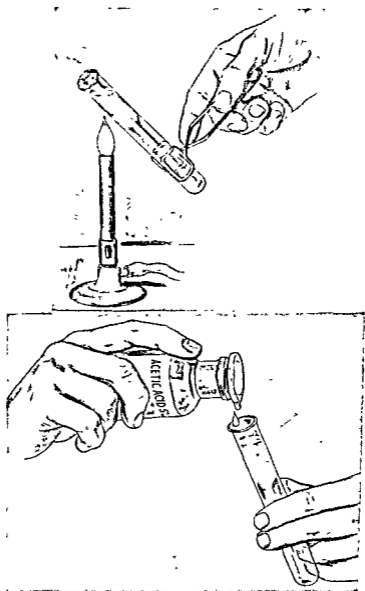


Fig. 51. Technic for determining the presence of albumin in the urine
(Courtesy of Sharp and Dohme, Philadelphia)

excretion, the two acid products must be neutralized and therefore deplete the body of its alkali reserve, causing an acidosis.

7. Why is caffeine often included in drugs and medications that are taken by mouth?
8. The color of a twenty-four urine specimen is directly proportional to the volume. Explain why this statement is true.
9. Under what conditions would you expect an increase in the acidity of the urine? An alkaline urine?
10. How are the volume, the color, and the specific gravity of urine related to each other?
11. A urine specimen has a specific gravity of 1.022. Approximately how many grams of solids would a liter of this urine contain?
12. If a certain diet caused a definite increase in the amount of urea excreted in twenty-four hours, how would it probably affect the excretion of uric acid? Of creatinine? Of phosphates?
13. Why does a high protein diet increase the daily excretion of ammonia in the urine? Of sulfates?
14. In general what effect would a vegetarian diet have on the excretion of the normal constituents of urine?
15. How is the excretion of phosphates and of ammonia related to the acid-base balance of the body?
16. If a routine examination of a urine specimen revealed a positive Benedict test how would you proceed to determine if the patient had diabetes mellitus? (use only tests on urine)
17. Pregnant or nursing women often excrete sugar in the urine. What is the nature of the sugar? Why is this sugar excreted at this particular time?
18. Why is albumin normally not present in the urine? Under what conditions may it be excreted?
19. If a urine specimen gave a positive test for the acetone bodies, under what conditions would you suspect diabetes mellitus? Under what conditions would you rule out diabetes mellitus?
20. A positive test for bile in the urine would probably indicate what condition? Why?
21. List four conditions in which blood would be present in the urine.
22. Of what value to the clinician is a kidney function test? What is the principle of such a test?

may be detected by adding a solution of benzidine followed by a few drops of hydrogen peroxide. If blood is present, a blue color develops.

KIDNEY FUNCTION TESTS

Many tests have been devised to determine how effectively the kidneys function. Two of these tests will be discussed briefly.

Phenolsulfonephthalein Test

Phenolsulfonephthalein or *phenol red* is a nontoxic dye that is rapidly excreted by the kidneys after it is injected into the blood stream. Urine specimens are collected at intervals after the injection and the amount of the dye in the urine is determined colorimetrically. Normally functioning kidneys will excrete 60 to 85 per cent of the dye within two hours. This test for kidney function is perhaps the most widely used in clinics.

Urea Clearance Test

In the urea clearance test, a comparison is made between the concentration of urea in the blood and the rate of its excretion in the urine. By determining the urea in the blood and urine at intervals, the number of cubic centimeters of blood that is cleared of urea in a given time can be calculated. Normally the kidneys clear about 65 to 100 cc. of blood of urea in one minute. This value will be lower if the kidneys are diseased.

REVIEW QUESTIONS

1. List several functions of the kidney.
2. Outline the essential processes in the formation of urine.
3. What is a Malpighian corpuscle? A tubule? The glomerulus?
4. Why are threshold substances such as glucose and amino acids reabsorbed into the blood stream? What reason would you suggest for calling these substances threshold substances?
5. In an accurate examination of the urine why is it important to collect a twenty-four-hour specimen?
6. Differentiate between the following terms: oliguria, anuria, and polyuria. Which term would you associate with each of the following conditions: diabetes insipidus, nephritis, and diarrhea?

an infectious agent as many believed. He cured the disease in chickens by feeding an extract of the rice polishings, the rice bran that forms a coating around each kernel of rice. He was one of the first investigators to use experimental animals for vitamin studies, and thus paved the way for countless future experiments.

About 1911, Funk, a Polish chemist, claimed that the deficiency diseases scurvy and beriberi were caused by the absence of a definite chemical substance from the diet. He succeeded in isolating a crystalline substance from extracts of rice polishings that was very active in preventing and curing beriberi. Since this substance was an amine, he suggested that these essential chemical substances be called "vitamines," from vital amines.

A few years later, other investigators found that certain animal fats such as butter and cod liver oil were capable of promoting growth in young rats fed a purified diet. Since the amine that prevented beriberi was soluble in water and since this substance was soluble in fat, the existence of at least two accessory food factors was suggested. McCollum designated these substances as *fat-soluble A* and *water-soluble B*, respectively. About 1920, when a third factor was established that prevented and cured scurvy, it was suggested that the terminology of Funk and McCollum be combined. Since only water-soluble B was related to amines the letter "e" was dropped from vitamine and the letters were added to give the new terms, vitamin A, vitamin B, and vitamin C. The alphabet of vitamins increased as new factors were discovered.

At the present time, we have over fifteen factors that are included in the category of vitamins. These are commonly classified as either water-soluble or fat-soluble. Among the water-soluble vitamins are included thiamine (vitamin B₁), riboflavin (vitamin B₂), nicotinic acid, pyridoxine (vitamin B₆), pantothenic acid, choline, inositol, *p*-aminobenzoic acid, biotin (vitamin H), and ascorbic acid (vitamin C), while the fat-soluble vitamins include vitamins A, D, E, and K. Many of these factors have been crystallized and their chemical nature determined. The modern trend, therefore, is to designate vitamins by their

CHAPTER XXII

Vitamins

DURING the past thirty years, the most important progress in the study of nutrition has been in the field of *vitamins*. Until early in the twentieth century it was believed that an adequate diet consisted of sufficient carbohydrates, fats, proteins, and inorganic salts. When animals were placed on a purified diet containing these constituents, however, they showed poor development unless they were given additional foods, such as milk. These additional foods were thought to contain "accessory food factors" that were needed in small amounts for proper nutrition.

What we now recognize as vitamin deficiency diseases have been observed for centuries, but very little progress has been made in their treatment until recent years. Records show that the Crusaders suffered from *scurvy*. This disease was widespread among sailors on early sailing vessels because of the lack of fresh foods. As early as 1720, citrus fruits were used as a cure for scurvy. The fact that all British ships were later required to carry stores of lime juice to prevent scurvy on long voyages led to the use of the terms, "limey" for sailors, "lime juicers" for ships, and "lime-house district" for the section of the town in which the sailors lived. Another disease that occurred particularly among sailors on Japanese ships was *beriberi*. In 1882, one of their medical officers found that beriberi could be prevented by including fruits, vegetables, barley, and meat in the sailors' diet.

In 1897, Eijkman, a Dutch physician working in the East Indies, proved that beriberi was due to a faulty diet instead of

of this vitamin, pyruvic acid is not broken down and accumulates in the blood and tissues. The neuritis that commonly occurs with thiamine deficiency is thought to be due to the accumulation of pyruvic acid. Recently large doses of thiamine have been successfully used in the treatment of several cases of neuritis. *Alcoholic polyneuritis* commonly occurs in people who



Fig 52 Atrophic beriberi. Note extensive atrophy of the arm and leg muscles. (From Funk and Dubin: *The Vitamines*. Baltimore, Williams and Wilkins Co.)

drink excessive amounts of alcohol. The food intake is diminished in such cases because the alcohol satisfies the appetite, therefore the thiamine intake is decreased and polyneuritis results. Pregnancy and lactation may be accompanied by neuritis, since the demand for the vitamin is high and the food intake may be restricted by nausea and vomiting.

chemical names rather than by letters. The water-soluble and fat-soluble vitamins listed above are essential to our knowledge of nutrition and will be discussed in more detail.

WATER-SOLUBLE VITAMINS

VITAMIN B COMPLEX

As has already been stated, the first vitamin to be recognized was water-soluble B or vitamin B. Because this vitamin has been shown to consist of several dietary factors, it is now called the *vitamin B complex*. As new members of this group were discovered they were designated by subnumbers as B₁, B₂, B₃, etc. Other factors of the B complex were originally known as vitamin G and vitamin H. To overcome the confusion of nomenclature, we commonly call these vitamins by their chemical names, for example vitamin B₁ is thiamine, vitamin B₂ is riboflavin, and so on.

Thiamine

Effects of Deficiency. Some of the early symptoms that develop on a thiamine-deficient diet are loss of appetite (anorexia), fatigue, loss of weight, and constipation due to decreased motility of the stomach and intestines. Administration of thiamine preparations causes a marked increase in appetite, and an improvement in the condition of constipation. Thiamine is a stimulant to the appetite only when the anorexia is due to lack of this vitamin.

As the deficiency progresses, a nervous disease called *polyneuritis* in animals and *beriberi* in man develops. This disease, involving the peripheral nerves of the body, is first evidenced by cramps in the muscles, numbness of the extremities, and pain along the nerves. Later the nerves become very painful, and the muscles become paralyzed and atrophied from disuse. Edema, or swelling of the muscles of the arms and legs, and circulatory disturbances are common in advanced beriberi. The heart enlarges and finally death occurs from heart failure.

It has been generally accepted that thiamine is essential to normal oxidation of carbohydrates in the body. In the absence

ties of this vitamin are taken in excess of body needs, it is excreted in the urine.

The requirements of most people for this vitamin can be met by a daily intake of 1 to 2 mg. of thiamine. During pregnancy and lactation, this amount should be increased to 2 to 3 mg. per day.

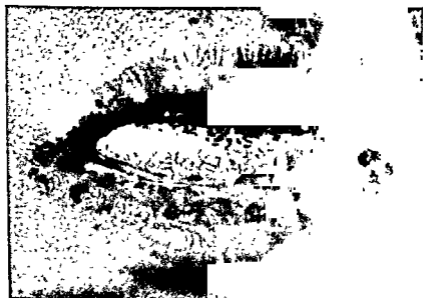
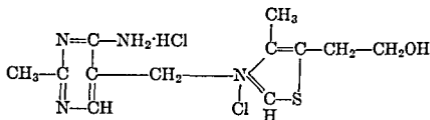


Fig. 53. The effect of a riboflavin deficiency on the lips and tongue. (From Bicknell, F., and Prescott, F.: *The Vitamins in Medicine*. London, Wilham Heinemann Medical Books, Ltd.)

Riboflavin

Effects of Deficiency. Until recently, the need for riboflavin (vitamin B₂ or G) in human nutrition has not been definite. If this vitamin is lacking from the diet for long periods of time, characteristic symptoms occur. Among these are cracks and sores on the lips and in the corners of the mouth. The eyes show dimness of vision, sensitivity to light, and inflammation of the cornea. Animals such as the rat, dog, chicken, and pig develop definite symptoms on riboflavin-deficient diets. For example, in rats, such a diet causes loss of hair, failure to grow, and cataracts of the lenses of the eyes, while dogs exhibit loss of weight, vomit-

Chemical Nature. The formula for thiamine was established in 1936, when it was synthesized. It consists of a pyrimidine ring and a sulfur-containing thiazole ring joined as shown below:



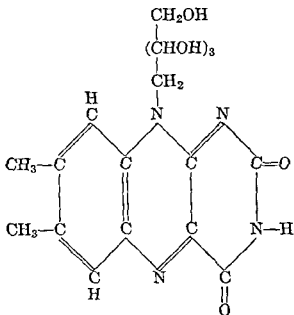
Thiamine (Hydrochloride)

This formula represents the hydrochloride salt; it is in this form that the synthetic vitamin is administered. The vitamin is soluble in water, dilute alcohol, and acids, and may be heated in an acid solution with little loss of potency. When heated in an alkaline solution, it rapidly loses its activity. Ordinary cooking procedures destroy 10 to 50 per cent of the thiamine. The loss of thiamine is greatly increased when sodium bicarbonate is added to preserve the color of green vegetables during cooking.

Occurrence. Brewers' yeast, wheat germ, eggs, meat (pork), and whole grains are good sources of thiamine in foodstuffs. Milk, vegetables, and fruits are fair sources, while milled cereals such as white flour are very poor sources of the vitamin. At the present time, large quantities of synthetic thiamine are being used in the fortification of white flour and other commercial foods.

Requirements. The daily requirement for thiamine depends somewhat on the type of diet consumed by a person. It has already been shown that thiamine is necessary for normal carbohydrate metabolism; it is also probably used in the catabolism of excess protein for the production of energy. A person who consumes a high carbohydrate and protein diet requires an abnormally large amount of this vitamin, while a high fat diet has a sparing action on thiamine. Since very little storage of thiamine occurs in the body, a thiamine-deficient diet will produce typical symptoms within ten to thirty days. When quan-

eggs, beef muscle, and leafy vegetables are good sources of this vitamin. Milled cereal products lose their riboflavin, and at present the trend is toward the fortification of white flour with riboflavin as well as with thiamine.



Riboflavin

Requirements. A daily intake of 2 to 3 mg. of riboflavin has been recommended by physicians. Riboflavin can be stored to a limited extent, but excessive amounts are merely excreted in the urine.

Nicotinic Acid

Effects of Deficiency. Lack of nicotinic acid causes *pellagra* in man and blacktongue in dogs. Pellagra is a disease characterized by skin lesions that develop on parts of the body that are exposed to sunlight. Sore and swollen tongues, loss of appetite, diarrhea, nervous and mental disorders are typical symptoms of pellagra.

Nicotinic acid plays a role similar to riboflavin in oxidation-reduction reactions in the tissues. It is a constituent of an

ing, diarrhea, muscular weakness, and death. Riboflavin is an essential constituent of the yellow enzyme, which is necessary for the proper oxidation of carbohydrates and proteins in the tissue cells.

Chemical Nature. Riboflavin is an orange solid that is slightly soluble in water and alcohol, giving a greenish yellow fluorescent



Fig. 54. The eyes and mouth in a riboflavin deficiency. (From Bicknell, F., and Prescott, F.: *The Vitamins in Medicine*. London, William Heinemann Medical Books, Ltd.)

solution. It is composed of ribose (a pentose) and flavin (a pigment), as shown in the following formula. The vitamin is stable to acids and heat but is destroyed by light and alkalis. From 10 to 20 per cent of riboflavin in foods may be destroyed by cooking.

Occurrence. Riboflavin, closely related to thiamine, is found in many of the same sources. For example, brewers' yeast, liver,

enzyme system that is essential in the oxidation of glucose in the body and in the fermentation of glucose by yeast.

Chemical Nature. Nicotinic acid is a simple derivative of pyridine. It is soluble in water and dilute alcohol and is stable to acid, alkalies, heat, and light. The amide of nicotinic acid is also effective in the treatment of pellagra and is the form that is used clinically.

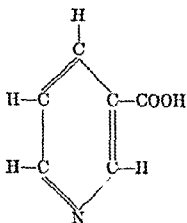
Occurrence. Liver, lean meat, and yeast are good sources of nicotinic acid while corn, molasses, and fat meat are very poor sources. Because the latter three foods are the major constituents of the diet of the poorer classes in the South, pellagra is prevalent throughout that region. Nicotinic acid as a chemical has been known for many years and is readily obtainable. The synthetic vitamin is used in large amounts to fortify white flour. The similarity of the terms nicotine and nicotinic acid caused laymen to call bread baked with fortified flour "tobacco bread." To overcome the commercial disadvantage of such a term, the name "niacin" was coined for nicotinic acid.

Requirements. The daily recommended requirement for humans is 10 to 30 mg. of nicotinic acid or nicotinic acid amide. While this vitamin is specific for pellagra, most cases of this disease require additional thiamine and riboflavin for a complete cure, because of a multiple deficiency.

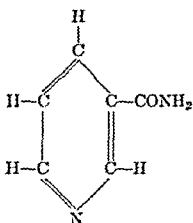
Pyridoxine

Effects of Deficiency. The need for pyridoxine (vitamin B₆) has not definitely been established for humans. In cases of pellagra that have not been completely cured by treatment with nicotinic acid, thiamine and riboflavin, the administration of pyridoxine has been effective in relieving the persisting symptoms. The rat is particularly sensitive to the lack of this vitamin. It develops a dermatitis of the paws, nose, lips, chin, and sides of the face, called *acrodermia*.

Chemical Nature. Pyridoxine is related to nicotinic acid in that it also is a pyridine derivative. It is stable to acids, alkalies, and heat and is soluble in water and alcohol.



Nicotinic Acid



Nicotinic Acid Amide



Fig. 55. Pellagra in a child. Extensive pigmentation occurs on areas that are exposed to the light. (From Bicknell, F., and Prescott, F.: *The Vitamins in Medicine*. London, William Heinemann Medical Books, Ltd)

synthesized. It is soluble in water and stable to heat in neutral solutions, but is readily hydrolyzed by boiling in acid or alkali. The calcium salt of the vitamin is available commercially.

Occurrence. Brewers' yeast, liver, and eggs are rich sources of pantothenic acid; whole grains, meats, butter, and milk are good sources. As in the case of pyridoxine, no daily requirement

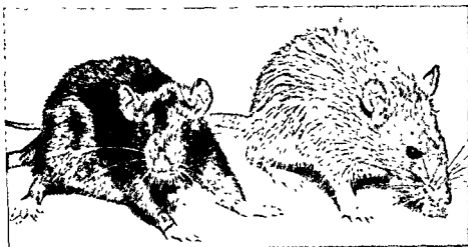
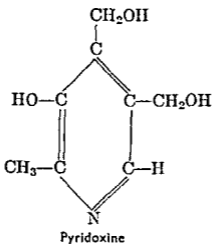


Fig. 56. Pantothenic acid deficiency in rats. The rat on the right shows a definite greying of the hair on the deficient diet. The animal on the left is a control and received this vitamin in its diet. (Courtesy of Research Laboratories, S. M. A. Corporation.)

for humans has been established. About 10 mg. a day has been proposed as adequate.

Choline

Effects of Deficiency. A choline-deficient diet will cause an excessive accumulation of fat in the liver (fatty livers) and hemorrhage of the kidneys in young, rapidly growing rats. The fatty livers that develop in young rats and other animals on a choline-free diet may be due to the failure to form sufficient phospholipids for the transportation of fats in the body. Diets deficient in choline also affect the process of lactation in rats, stop hens from laying eggs, and cause lack of appetite in young dogs.

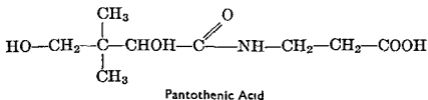


Occurrence. Brewers' yeast, liver, wheat bran, meats, and milk are good sources of pyridoxine. It has been synthesized and is available in the pure form. As yet no figure has been given for the daily human requirements of pyridoxine, although it has been suggested that 1 to 2 mg. are necessary.

Pantothenic Acid

Effects of Deficiency. There is no satisfactory evidence at present that pantothenic acid is required by man. A deficiency of this vitamin in chicks results in a dermatitis around the mouth and a retardation of growth and feathering. A prolonged deficiency results in death. The black fur on certain rats and foxes turns grey on a pantothenic acid-deficient diet (Fig. 56). The color is restored when this substance is administered. Although there are preparations containing pantothenic acid sold for the cure and prevention of grey hair in humans, no satisfactory proof exists for their effectiveness.

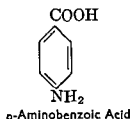
Chemical Nature. The structural formula for pantothenic acid has been recently worked out and the compound has been



Para-aminobenzoic Acid

Effects of Deficiency. A diet deficient in *p*-aminobenzoic acid retards the growth of young chickens, causes grey hair in black rats and mice, and prevents bacterial multiplication. There is some evidence that grey hair in man may be caused by the lack of vitamins, but experiments with both *p*-aminobenzoic and pantothenic acids have failed to yield promising results. It has been claimed that *p*-aminobenzoic acid is essential for the normal pigmentation of the skin.

Chemical Nature. This compound, known to chemists for many years, has a fairly simple structure. As yet no relationship has been found between *p*-aminobenzoic acid and human nutrition.

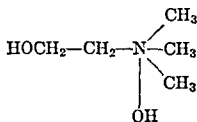


Since the advent of sulfa drugs, it has been found that this vitamin interferes with the therapeutic action of sulfanilamide. These two compounds are very similar in structure and apparently both fit into an enzyme system in bacteria. Sulfanilamide and the other sulfa drugs stop the action of pathogenic bacteria when present in this enzyme system and are called *bacteriostatic agents*.

Biotin

Effects of Deficiency. When rats are fed large quantities of raw egg white, they develop a dermatitis around the mouth and show a loss of hair. The addition of biotin to such diets prevents the occurrence of these symptoms. None of these symptoms have been induced in rats on a biotin-deficient diet in which proteins other than raw egg white were fed, although there is some evidence that hamsters will exhibit characteristic symp-

Chemical Nature. Choline is a strongly alkaline substance



Choline

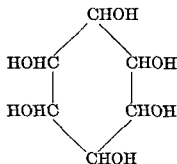
soluble in water and alcohol. It is readily available, having been synthesized long before it was known to act as a vitamin.

Occurrence. Choline occurs as a constituent of lecithin in all living cells. Meats such as brain, liver, kidney, and sweetbreads are rich sources of this vitamin. There is no evidence at present that choline is required in human nutrition.

Inositol

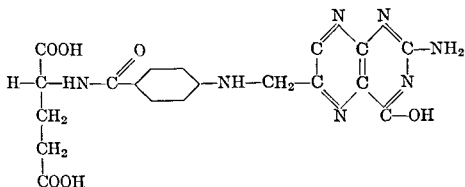
Effects of Deficiency. A synthetic diet containing all the known vitamins failed to support growth in young mice and caused a loss of the hair. The administration of inositol cured both of these symptoms. The condition of "spectacled eyes" in rats is prevented by inositol in the diet.

Chemical Nature. Inositol is a white crystalline solid with the following composition:



Inositol

Occurrence. The best sources of inositol are muscle tissue, liver, brain, and kidneys. This vitamin has not been suggested as an essential constituent of the human dietary.



Folic Acid

It is a yellow compound only slightly soluble in water and stable to heat in neutral or alkaline solutions but not in an acid solution.

Occurrence. Folic acid occurs in many plant and animal tissues, especially in the foliage of plants, from which it was named. Yeast, soybeans, wheat, liver, kidney, and eggs are good sources of this vitamin.

Requirements. No specific requirement of folic acid has been established for humans, although from 100 to 200 mg. per day are given in the treatment of macrocytic anemias.

Other Vitamins of the B Complex

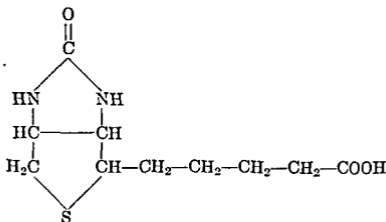
There are many other factors that have been found essential for the growth of animals, yeasts, and bacteria but have not been definitely established in nutrition to the extent where they are included in the above group of vitamins.

OTHER WATER-SOLUBLE VITAMINS

Ascorbic Acid

Effects of Deficiency A deficiency of ascorbic acid (vitamin C) in the diet results in the disease known as *scurvy*. Early symptoms are loss of weight, anemia, and fatigue. As scurvy becomes more severe, the gums become swollen, bleed readily, and the teeth loosen. The bones become brittle and are easily broken. Hemorrhages develop under the skin and in the mucous membrane. In the later stages, the teeth fall out. The joints become

toms on a similar diet. Biotin has been found essential for the normal growth of yeast, bacteria, and fungi.



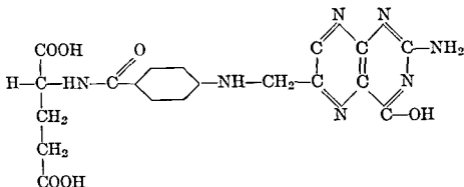
Biotin

Chemical Nature. Biotin is a sulfur-containing compound that is stable to heat and light and ordinary chemicals, but is hydrolyzed by strong acids or alkalies. The role of biotin in human nutrition has not been established at present.

Folic Acid

Effects of Deficiency. A lack of this vitamin in the diets of young chickens and monkeys causes anemia and other blood disorders. The beneficial effects of folic acid in the treatment of anemia in animals led to a study of its effectiveness in various types of anemia in man. Recently, favorable clinical results have been reported after the use of this vitamin in *macrocytic anemias*, which are characterized by the presence of giant red corpuscles in the blood. This type of anemia may occur in sprue, pellagra, pregnancy, infancy, and in gastric and intestinal disorders.

Chemical Nature. The structural formula for folic acid has recently been reported and is a complex molecule consisting of three major parts. Since it is composed of a yellow pigment called a pteridine, *p*-aminobenzoic acid, and glutamic acid, the vitamin is often called *pteroylglutamic acid*.



Folic Acid

It is a yellow compound only slightly soluble in water and stable to heat in neutral or alkaline solutions but not in an acid solution.

Occurrence. Folic acid occurs in many plant and animal tissues, especially in the foliage of plants, from which it was named. Yeast, soybeans, wheat, liver, kidney, and eggs are good sources of this vitamin.

Requirements No specific requirement of folic acid has been established for humans, although from 100 to 200 mg. per day are given in the treatment of macrocytic anemias.

Other Vitamins of the B Complex

There are many other factors that have been found essential for the growth of animals, yeasts, and bacteria but have not been definitely established in nutrition to the extent where they are included in the above group of vitamins

OTHER WATER-SOLUBLE VITAMINS

Ascorbic Acid

Effects of Deficiency A deficiency of ascorbic acid (vitamin C) in the diet results in the disease known as *scurvy*. Early symptoms are loss of weight, anemia, and fatigue. As scurvy becomes more severe, the gums become swollen, bleed readily, and the teeth loosen. The bones become brittle and are easily broken. Hemorrhages develop under the skin and in the mucous membrane. In the later stages, the teeth fall out. The joints become

very painful, headaches and convulsions develop, and the patient may die in a delirium.

One of the essential functions of ascorbic acid is the formation and maintenance of the intercellular substance that cements the cells together. This *intercellular tissue* is particularly important in the capillary walls, cartilage, bones, and teeth. On a diet lacking ascorbic acid, the intercellular substance is lost and structural weakness of capillary walls, bones, and teeth develop. Since the hemorrhage of small capillary blood vessels occurs early in the disease, capillary resistance tests are often used to



Fig. 57. Gingivitis caused by a lack of ascorbic acid in the diet. (From Bicknell, F., and Prescott, F.: *The Vitamins in Medicine*. London, William Heinemann Medical Books, Ltd.)

detect the early stages of scurvy. These tests are carried out by increasing the intravascular pressure with a tourniquet and observing the skin for hemorrhage spots. Extreme scurvy is not commonly seen today, although many cases of subacute or latent scurvy are recognized. Symptoms such as sore receding gums, sores in the mouth, tendency to fatigue, lack of resistance to infections, defective teeth, and pains in the joints are indicative of subacute scurvy.

Man, monkeys, and guinea pigs are the only species that are known to be susceptible to the lack of ascorbic acid. Other animals apparently possess the ability to synthesize this vitamin.

Chemical Nature. Ascorbic acid, a simple compound with six carbon atoms, is an oxidation product of a hexose sugar.

The hydrogen atoms on the second and third carbon atoms (from the top) are readily removed by oxidation, forming a ketone called *dehydroascorbic acid*. This reaction is reversible and either compound may be formed from the other. Because of this oxidation-reduction relationship, ascorbic acid probably functions in oxidations and reductions in the body tissues.

Ascorbic acid is a strong reducing agent that is readily destroyed by heat in the presence of atmospheric oxygen. This

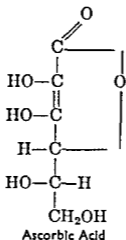


Fig. 58. Hemorrhages under the skin in scurvy. (From Duncan, G. G. *Diseases of Metabolism*. Philadelphia, W. B. Saunders Company.)

oxidative destruction is accelerated in alkaline solution and by certain metals such as copper

Occurrence. The richest sources of vitamin C are paprika and citrus fruits such as lemons, oranges, and grapefruit. Tomatoes, raw cabbage, strawberries, and green leafy vegetables are good sources of this vitamin, while cereals, meats, eggs, and milk are poor sources.

A large percentage of the ascorbic acid in foods is destroyed or lost in cooking. Boiling for thirty minutes will destroy 70 to 90 per cent of the vitamin C content of cabbage and green vegetables. The addition of sodium bicarbonate to maintain the green color of vegetables further increases the loss.



Requirements. In comparison with other vitamins, large amounts of ascorbic acid are required daily. It has been recommended that 70 to 80 mg. of this vitamin per day would constitute an adequate intake. This amount should be increased during pregnancy and lactation.

THE FAT-SOLUBLE VITAMINS

Vitamin A

Effects of Deficiency. A diet deficient in vitamin A will not support growth, a fact which led to its discovery. The lack of this vitamin causes other more specific symptoms; for example, it affects the epithelial cells of the mucous membrane of the eye, the respiratory tract, the digestive tract, and the genito-urinary tract. When the epithelial cells lose their ability to secrete normally, the mucous membrane hardens and dries up, a process known as *keratinization*. The eye is first to show the effect of a deficiency and develops a disease called *xerophthalmia*. This disease is characterized by inflamed eyes and eyelids. The eyes finally become infected and when this infection involves the cornea and lens, sight is permanently lost. A continued deficiency of vitamin A results in extensive infection in the respiratory tract, the digestive tract, and the urinary tract. This vitamin has often been called the *anti-infective* vitamin because it prevents infections that are caused by the drying of mucous membrane. It should be emphasized that this vitamin is not

anti-infective in the sense that it combats the infectious organisms, but because it maintains a healthy condition of the mucous membrane Vitamin A deficiency also causes sterility since it affects the lining of the genital tract. It is therefore necessary for normal reproduction and lactation.

One of the first symptoms of the lack of vitamin A is *night blindness*. The retina of the eye contains a pigment called visual



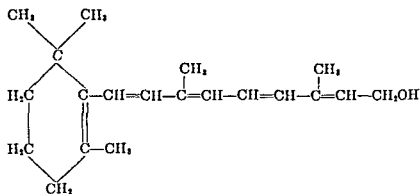
Fig. 59. Xerophthalmia in an infant. (From Marriot, W. K., and Jeans, P. C.: *Infant Nutrition*. St. Louis, C. V. Mosby Company.)

purple, a protein combined with vitamin A, responsible for vision in dim light. This pigment is bleached on exposure to light and is regenerated only slowly in the absence of this vitamin. The eye is therefore unable to adapt itself to rapid changes of light and the vision is impaired. Recent studies indicate that night blindness is more common than was formerly suspected.

Chemical Nature. Vitamin A is closely related to a group of pigments called carotenoids. The pigments occur widely in plants

and include the carotenes, which are responsible for the color of yellow corn, carrots and butter. Four of these pigments, alpha-, beta-, and gamma-carotene and cryptoxanthin, can be converted into vitamin A in the animal body. This vitamin is soluble in fat and fat solvents and is a liquid at room temperature. It has recently been synthesized.

Chemically it represents one-half of the beta-carotene molecule ($C_{40}H_{56}$) with the end carbons oxidized to form a primary alcohol group.



Vitamin A

Vitamin A is stable to heat, acids, and bases but not to oxidation. Thus, when fats become rancid through oxidation, the vitamin A content is destroyed. Ordinary methods of cooking do not appreciably reduce the vitamin A content of foods.

Occurrence. Food sources of the vitamin consist of the four carotenoid pigments in plants and the free vitamin in animal products. No differentiation will be made between the two forms in this discussion. Fish liver oils are very potent sources of vitamin A. Eggs, liver, milk and dairy products, green vegetables, and tomatoes are good food sources of the vitamin.

The body has the ability to store vitamin A in the liver when it is present in the food in excess of the body requirements. Infants obtain a store of the vitamin in the first milk (colostrum) of the mother, which is 10 to 100 times as rich in vitamin A as ordinary milk.

Requirements. The recommended daily requirement of vitamin A is approximately 5000 international units (3 mg. of beta-

carotene). This value is increased to about 8000 international units a day during pregnancy. One to two teaspoons of cod liver oil would furnish the normal daily requirement of this vitamin.

Vitamin D

Effects of Deficiency. The lack of vitamin D in the diet of infants and children results in an abnormal formation of the



Fig. 60. Rickets. Square head, and beaded ribs (rachitic rosary). (From Mitchell's *Pediatrics and Pediatric Nursing* revised by Lyon, R. A., and Kaltenebach, W., Philadelphia, W. B. Saunders Company.)

bones, a disease called *rickets*; therefore the vitamin is often known as the *antirachitic vitamin*. Calcium and phosphorus, the most important mineral elements present in bone, and vitamin D, are all involved in proper bone formation. In rickets, the bones are improperly calcified and are weak and soft. The weight of the body causes the legs to bow. The joints become enlarged and the ribs become beaded, forming the familiar "rachitic

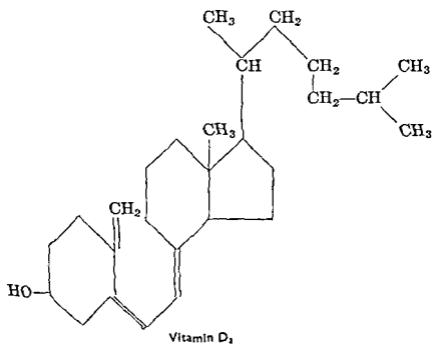
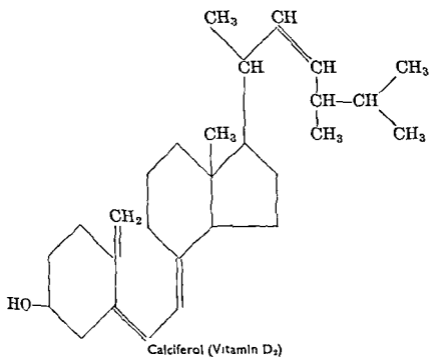
rosary," or they may become deformed, producing the condition known as "pigeon breast." This malformation of the chest combined with weak abdominal muscles causes a potbellied appearance.

Rickets does not occur in adults after bone formation is complete, although the condition of *osteomalacia* may occur in women after several pregnancies. In *osteomalacia*, the bones soften and abnormalities of the bony structure may occur. Vitamin D deficiency is also associated with poor tooth development. Since the composition of bones and teeth are similar, it is not surprising that a lack of this vitamin during formation of the permanent teeth will result in defective teeth. Tooth decay (dental caries) has been reduced considerably by the administration of sufficient vitamin D during childhood.

Chemical Nature. Several compounds with vitamin D activity exist, although only two of them commonly occur in antirachitic drugs and foods. These two compounds are produced by the irradiation of ergosterol and 7-dehydrocholesterol with ultraviolet light. Ergosterol is a sterol that occurs in yeast and molds, while 7-dehydrocholesterol is found in the skin of animals. Irradiated ergosterol is called *calciferol* or vitamin D₂; irradiated 7-dehydrocholesterol is called vitamin D₃. The structures of the two forms of vitamin D are very similar, as shown on page 283.

Occurrence. The fish liver oils are the most potent sources of vitamin D, while fish such as sardines, salmon, and herring are the richest food sources. Although eggs and butter contain appreciable quantities of the vitamin, the majority of foods are very low in vitamin D. For this reason, children are given additional amounts of this substance in their diet.

The ultraviolet rays in sunlight form vitamin D by irradiation of 7-dehydrocholesterol in the skin; thus children who play outdoors in the summer or are exposed to ultraviolet lamps materially increase the vitamin D content of their bodies. If their diet contains sufficient calcium and phosphorus, bone formation will proceed normally. It should be emphasized that sunshine or vitamin D will not take the place of these two mineral elements in the diet. The main function of vitamin D in the



body is to increase the utilization of calcium and phosphorus in the formation of bones and teeth.

Irradiation of foods is often used to increase their vitamin D content. Milk may be irradiated or a small amount of irradiated ergosterol may be added. Several products on the market today have their vitamin D content increased in this manner. In addition to fish liver oils, more potent sources of vitamin D such as calciferol, viosterol and drisdol (all three from irradiated ergosterol) and liver oil concentrates are on the market.

Requirements. The daily requirements for vitamin D in young children may be met by 10 to 20 micrograms of the pure vitamin, which is equivalent to 400 to 800 international units. This amount should be sufficient for older children and adults, although the adult requirement is not agreed upon. This amount of vitamin D cannot be supplied by an ordinary diet so additional sources of the vitamin must be given to growing children and to women during pregnancy and lactation.

Vitamin E

Effects of Deficiency. A diet deficient in vitamin E produces sterility in animals. The male rat, for example, loses his ability to make spermatozoa, and continued lack of this vitamin results in permanent sterility. The female rat shows a normal ovulation and mating. The fetuses grow for about two weeks, at which time they die and are resorbed by the female. If sufficient vitamin E is given after resorption occurs, the female rat recovers and may give birth to a normal litter after another mating.

A lack of vitamin E results in the condition of *muscle dystrophy* in such animals as the rat, rabbit, dog, and hamster. Muscle dystrophy is characterized by degenerative changes in the muscle fibers, resulting in paralysis. The administration of vitamin E will cure the condition in its early stage.

Chemical Nature. Vitamin E is related to a group of compounds called tocopherols. At least three, alpha-, beta-, and gamma-tocopherol, have vitamin E activity. Alpha-tocopherol is the most potent and has recently been synthesized. Vitamin E is stable to heat but is destroyed by oxidizing agents and ultra-

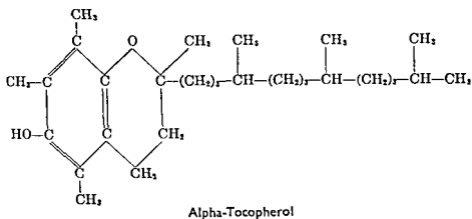


Fig. 61. Hemorrhage in a three-day-old infant caused by the lack of vitamin K. The right arm and shoulder and the umbilical cord show evidence of hemorrhage (From Bicknell, F, and Prescott, F.: *The Vitamins in Medicine*. London, William Heinemann Medical Books, Ltd)

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SUMMARY OF IMPORTANT VITAMINS IN HUMAN NUTRITION

Vitamin	Main Deficiency Symptoms	Function in the Body	Average Daily Requirement	Good Sources
B ₁ , thiamine	Beriberi	Oxidation of carbohydrates	1-2 mg.	Yeast and wheat bran
B ₂ , riboflavin	Cracked, sore lips, impaired vision	Oxidation in the tissues	2-3 mg.	Yeast and liver
Nicotinic acid	Pellagra	Oxidation in the tissues	10-30 mg.	Liver, meat and yeast
C, ascorbic acid	Scurvy	Maintenance of intercellular tissue	70-80 mg	Citrus fruits, tomatoes and cabbage
A, carotenes	Xerophthalmia, night blindness	Maintenance of normal epithelial cells	5000 I.U. 3 mg. beta-carotene	Fish liver oils and green vegetables
D, calciferol	Rickets	Regulates calcium and phosphorus metabolism	400-800 I.U. 10-20 μ g calciferol	Fish liver oils and fish
E, alpha-tocopherol	Sterility, muscle dystrophy (in animals)	Essential for normal muscle metabolism	Not known	Wheat germ oil and leafy vegetables
K	Increased clotting time of blood	Production of prothrombin	Not known	Alfalfa, spinach, and kale

violet light. Oxidative rancidity of fats rapidly destroys the vitamin potency.

Occurrence. The richest source of vitamin E is wheat germ oil. Other plant oils such as corn oil and cottonseed oil contain appreciable quantities of the vitamin. Green leafy vegetables, egg yolk, and meat are good sources of this substance.

Deficiency of Vitamin E in Humans. As yet evidence is not conclusive that vitamin E is required in human nutrition. Large doses of this vitamin in the form of wheat germ oil have been administered to women in an attempt to prevent habitual abortion. While the clinical evidence is meager, it is doubtful that habitual abortion is due to a dietary deficiency in view of the widespread distribution of vitamin E in nature.

Vitamin K

Effects of Deficiency. A diet lacking in vitamin K will cause an increase in the clotting time of the blood. This condition leads to the occurrence of hemorrhages under the skin and in the muscles. The abnormality in the clotting mechanism is due to a reduction in the formation of *prothrombin*, one of the factors in the normal process.

In man, obstructive jaundice reduces the prothrombin level of the blood because vitamin K cannot be properly absorbed from the intestine in the absence of bile. In these cases, post-operative hemorrhage is frequent, but it can be controlled if vitamin K and bile are given for several days before the operation. Other intestinal conditions that are accompanied by a low prothrombin level in the blood may be benefited by the administration of this vitamin.

Hemorrhages of newborn babies often result from injuries at birth, since the prothrombin level of infant blood is usually low. These hemorrhages have been controlled by giving vitamin K to the baby, or to the mother prior to childbirth.

Chemical Nature. Vitamin K, a derivative of 1, 4-naphtho-

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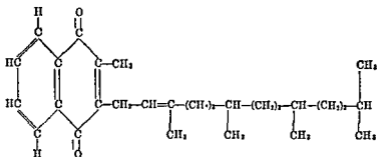
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Chemical Nature. Vitamin K, a derivative of 1, 4-naphtho-

12. What steps have been taken to prevent pellagra in the United States? What is niacin?
13. *Plan a simple experiment to determine whether pantothenic acid will prevent grey hair in humans.*
14. Solutions of pantothenic acid are sold for the prevention of grey hair. If you were to prepare a remedy for the loss of hair and the greying of hair what vitamins would you include in your preparation?
15. What are some of the symptoms of subacute scurvy? What common type of diet may produce subacute scurvy?
16. How does ascorbic acid function in the body?
17. Why is the modern trend toward cooking vegetables in as short a time as possible?
18. How would you characterize the disease called xerophthalmia?
19. Why is it misleading to advertise vitamin A as the anti-infective vitamin?
20. What is night blindness? This condition has been cured by the ingestion of large amounts of carrot juice. What source would be more convenient and more concentrated?
21. How are young babies protected against vitamin A deficiency?
22. Why is vitamin D known as the antirachitic vitamin?
23. What are the factors involved in the proper formation of bones and teeth?
24. Why is it unnecessary to feed cod liver oil to children in the summer time?
25. Why are children and pregnant women often given extra sources of vitamin D?
26. Vitamin E is often called the antisterility vitamin. What is the reason for such a term?
27. Recently several cases of muscle dystrophy in children have been attributed to the lack of vitamin E in the diet. How would you treat these cases?
28. What conditions are benefited by the administration of vitamin K?
29. How does vitamin K function in the body?
30. Make a list of the vitamins that are required by man and give the average daily requirement for each vitamin.

quinone, exists in at least two active forms. Vitamin K₁ is represented as shown below:



Vitamin K₁

Vitamin K is a fat-soluble substance and therefore is soluble in the ordinary fat solvents. It is stable to heat but is destroyed by alkalis, acids, oxidizing agents, and light.

Occurrence. Rich sources of vitamin K are alfalfa, spinach, cabbage, and kale. The bacteria present in putrefying fish meal are capable of synthesizing vitamin K and are potent sources of this vitamin.

REVIEW QUESTIONS

1. What two dietary deficiency diseases were known long before modern vitamin studies began? How were these diseases treated?
2. Who initiated the use of experimental animals in vitamin studies? What vitamin was he working with?
3. Why were vitamins originally called *vitamines*? What caused the "e" to be omitted from the name?
4. Why is the modern trend to designate vitamins by their chemical names rather than by letters?
5. List the important water-soluble vitamins. Which of these belong in the vitamin B complex?
6. Name several of the main symptoms that develop on a diet deficient in thiamine. What disease is associated with a lack of thiamine in the diet of man?
7. Why is thiamine frequently of value in the treatment of neuritis?
8. Name three dietary sources of thiamine. What is the average daily requirement for this vitamin?
9. What observations would lead you to conclude that a person lacked riboflavin in his diet?
10. Why is riboflavin sometimes used in the fortification of white flour?
11. Why is pellagra more prevalent in the South than in the North?

	breads, fats, and a moderate amount of sweets.
Vitamin D source	Children should be exposed to sunshine or be given fish liver oils, vitamin D concentrates, or vitamin D milk.

Further interest in the study of nutrition has come from those responsible for supplying adequate diets to members of our armed forces in many climates and under various battle conditions. The major factors that constitute a proper diet will be discussed separately in the following section.

CARBOHYDRATE REQUIREMENT

Carbohydrates are not essential dietary constituents, because they may be formed from certain amino acids and from the glycerol portion of fats. They furnish the major source of energy in the average diet, however, and add to the variety and palatability of the food. It has been estimated that over one-half of the energy supplied by the diet is due to the carbohydrates in the food. The cellulose portion of many fruits and vegetables is indigestible and makes up the bulk of the material in the large intestine after absorption has occurred. This roughage is essential for the prevention of constipation.

Energy Requirement

Since carbohydrates are used mainly for energy, it may be appropriate to consider the energy requirements of the body. The minimum amount of energy required by the body at rest, when no digestion or muscular movement is occurring, is called the basal energy requirement or more often the *basal metabolism*. It has been found that the energy production of the body is more closely related to the surface area of the body than to the weight. For convenience, the basal requirement is referred to as the *basal metabolic rate* (B. M. R.), which is the number of large calories eliminated from each square meter of body surface in one hour under the conditions outlined above. [The large calorie (Cal or calories) is the amount of heat energy required to raise the temperature of 1 liter of water 1 degree centigrade.] A series

CHAPTER XXIII

Nutrition

THE war and the rationing system were responsible for many people becoming conscious of the importance of nutrition. Until recent years, it was thought that the nutritional requirements of the body could be satisfied with generous amounts of carbohydrates, fats, proteins, inorganic salts, and water. We now know that in addition to the above substances the body must be supplied with a sufficient quantity of vitamins, and that the type of dietary fat and protein is important to ensure an adequate diet for a normal person. A certain amount of indigestible material or roughage should be present to prevent constipation, and the antiketogenic foods should approximately double the ketogenic foods to prevent ketosis. According to nutritional authorities, the following dietary plan will provide an adequate diet for the majority of people:

TYPE OF FOOD	RECOMMENDED CONSUMPTION
Eggs	One or two per day.
Milk	One pint or more daily for adults; one quart daily for children.
Meat	One serving per day. Liver and fish at least once a week.
Vegetables	Potatoes and two cooked vegetables daily. Yellow leafy and green vege- tables, cooked or raw, should be eaten frequently.
Fruits	One or more servings daily, cooked or raw. Citrus fruits once a day, if possible.
Remainder of diet	Selected according to taste. Will usually contain a large amount of cereals,

	bread, fats, and a moderate amount of sweets.
Vitamin D source	Children should be exposed to sunshine or be given fish liver oils, vitamin D concentrates, or vitamin D milk.

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of average basal metabolic rates has been determined for normal persons of all ages. The basal metabolic rate of a person is not considered abnormal unless it varies more than 10 per cent from the normal standard value. In general practice, basal metabolic rates are expressed as percentage variations from the normal, for example, a basal metabolic rate of $+5$ would indicate a value 5 per cent higher than the normal value for a specific sex and age,

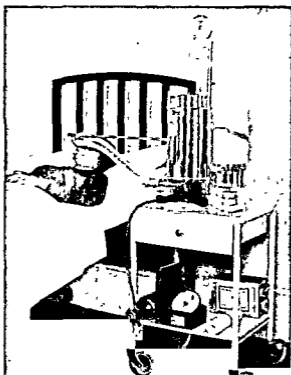


Fig. 62. Apparatus for the determination of the basal metabolic rate.
(Courtesy of Warren E. Collins, Inc., Boston.)

while a basal metabolic rate of -10 would represent a value 10 per cent below the normal standard.

The amount of energy required in a day consists of the basal requirement plus the energy expended for muscular activity. In addition to these two requirements, a source of energy must be supplied to account for the *specific dynamic action* in metabolism. Protein foods, especially, stimulate the rate of metabolism and require energy for their oxidation in the tissues. On an average

mixed diet, this energy for the specific dynamic action of foods amounts to about 10 per cent of the basal energy. The requirement for muscular activity obviously depends on the occupation of the person. Most professional people require between 500 and 1000 calories daily for this purpose. In general, a total daily energy requirement of from 2000 to 3000 calories will include the majority of the people in this class. In occupations where continuous hard physical labor is involved, the daily energy requirement may exceed 5000 calories.

LIPID REQUIREMENT

As yet, there is no definite evidence that lipids are required in the human dietary. It is reasonable to assume that on a lipid-free diet, the body would be unable to synthesize essential lipids such as lecithin, cephalin, sphingomyelin, and the cerebrosides. White rats, for example, on a lipid-free diet cease to grow, develop a dermatitis, and a characteristic scaly tail, and finally die. These symptoms may be prevented or alleviated by the presence of certain unsaturated fatty acids. These unsaturated fatty acids, called *essential fatty acids*, consist mainly of linoleic, linolenic, and arachidonic acids. White rats also require choline for normal nutrition and develop fatty livers when it is absent from the diet. Since choline is a constituent of the phospholipid lecithin, which is widely distributed in dietary fats, a choline deficiency in the human has not been recognized.

Lipids supply more than twice as much energy per gram as carbohydrates or protein. (The approximate energy value of 1 gm. of fat is 9 calories, of carbohydrates 4 calories and of protein 4 calories). About one-third of the calories of an adequate diet are supplied by lipids. From a practical standpoint, fats are the most economical source of energy, whereas proteins are the most expensive.

PROTEIN REQUIREMENT

Sufficient protein is required in the diet to provide adequate amounts of the essential amino acids for the growth of new tissues, the repair of old tissue, and the synthesis of hormones, enzymes, pigments, and similar substances. Growing children

require more protein than adults because they are continually forming new body tissue from the available amino acids.

Dietary proteins vary considerably in their content of the essential amino acids and may therefore be classed as adequate or inadequate. Plant proteins usually lack sufficient amounts of certain of the essential amino acids and as a general rule are more *inadequate proteins* than those from animal tissues. *Adequate proteins* are found in such animal products as eggs, milk, liver, and kidney, while the plant proteins present in cereals, vegetables, and legumes are termed inadequate. On a mixed diet, it is safe to include from 70 to 90 gm. of protein per day for an adult. Children require more protein and are usually fed 2 to 2.5 gm. of protein per kilogram of body weight compared to the value of slightly more than 1 gm. per kilogram for adults.

INORGANIC SALT REQUIREMENT

Of the inorganic substances required by the body, water is by far the most important. Many inorganic elements are essential for the normal functions of the body, and must be present in the diet. We will briefly discuss the requirements for some of the important mineral elements.

Calcium

Some of the major functions of calcium in the body include: (1) formation of bones and teeth, (2) clotting of blood, (3) formation of milk, (4) formation of calcium paracaseinate curd in digestion. Milk, probably the best source of dietary calcium, contains this element in a readily absorbable form, whereas the calcium of vegetables is sometimes absorbed with difficulty. The daily requirement for calcium is approximately 1.0 gm. for growing children and 0.7 gm. for adults.

Phosphorus

Since bones and teeth are composed mainly of a compound of calcium and phosphorus, this element is essential in their formation. An adequate amount of vitamin D is also required for proper calcium and phosphorus metabolism in the body.

Other functions of phosphorus are (1) formation of milk, (2) formation of organic phosphorus compounds such as phospholipids, nucleoproteins, and casein, (3) formation of phosphate buffers, and (4) formation of esters of phosphoric acid that function in the oxidation of carbohydrates. For maximum bone and tooth formation, the ratio of calcium to phosphorus in the diet should be approximately 2 to 1.

There are many foods that contain phosphorus, so a dietary deficiency of this element is much less likely than a deficiency of calcium. A daily intake of 1.3 gm. of phosphorus is thought to be adequate for children and adults.

Iodine

The main purpose of iodine in the body is in the development and functioning of the thyroid gland. As shall be seen later, a deficiency of this element results in hypothyroidism and simple goiter. The daily requirement of iodine is about 0.1 to 0.15 mg. Sea food and crops grown in coastal areas contain sufficient iodine to meet this requirement, but in the Great Lakes region the iodine content of the crops is extremely low. To overcome this deficiency and to prevent goiter, small amounts of an iodine salt (potassium iodide) are added to ordinary table salt.

Iron

Hemoglobin, the pigment of blood, requires iron for its formation in the body. A deficiency of this element results in anemia. Normally the body requires from 10 to 15 mg. of iron daily. This requirement is increased by menstruation, pregnancy, and lactation. The body of a newborn infant contains enough iron to last approximately six months. Since milk is deficient in this element, additional sources of iron must be fed after the first few months.

Copper

Copper is essential for the formation of hemoglobin. It probably acts as a catalyst because no copper is present in the pigment itself. Very small amounts of copper are required per day

(2 to 3 mg.) and it is doubtful that an ordinary diet would lack sufficient quantities of this element.

Sodium

The body requires sodium for several purposes. The buffer systems in the blood and tissue fluids are usually sodium salts, as for example, sodium bicarbonate and the sodium phosphates. The first named salt also produces the proper *pH* for enzyme action in the saliva and the pancreatic and intestinal juices. This element assists in the elimination of carbon dioxide by the lungs, and of acid products by the kidney.

The daily requirement of sodium, as sodium chloride, has been suggested as 1.7 gm. for children and 10 gm. for adults.

Potassium

Potassium is probably essential for proper cell formation in the body, since it occurs as a constituent of all animal cells. It functions with sodium in the relaxation of muscles. Salts of this element are found inside of the red blood cell, whereas sodium is present mainly in the blood plasma. Potassium therefore replaces sodium in the buffer salts used inside of the cells.

The requirement for this element may be met by a daily intake of 1.5 gm. for children and 3.0 gm. for adults.

VITAMIN REQUIREMENT

The vitamin requirement in human nutrition has been discussed in the preceding chapter. In the past few years, the use of vitamins and vitamin products by the general public has increased tremendously. It has been estimated that one-tenth of the retail drug business in the United States during 1946 was in synthetic vitamins and multiple vitamin preparations.

It cannot be stressed too strongly that adequate nutrition concerns food and not synthetic products that are taken as cure-alls. The proper source of vitamins in the diet is food, because there are many other requirements in an adequate diet besides vitamins.

GENERAL DIETARY REQUIREMENTS

In Pregnancy and Lactation

An adequate diet during pregnancy and lactation is essential for the development of the fetus, the placenta, the uterus, and breasts, and for the formation of milk. Obviously this calls for an increased intake of proteins. Inorganic salts and vitamin D are often given to pregnant women to insure proper bone development in the fetus.

In the Growing Child

An improper diet in childhood does not produce symptoms as striking as those shown in an infectious disease, but may result in far more serious handicaps when the child reaches maturity. Many of the common diseases that affect children are more prevalent among those suffering from malnutrition. The proper development of bones and teeth is closely related to an adequate intake of calcium, phosphorus, and vitamin D. The size of the adult body is partially hereditary, but may be influenced markedly by the diet in childhood. The malnutrition so extensive in Europe today is certain to influence the stature of the present generation of children.

In Disease and Abnormal Conditions in the Body

Variations in the diet are often advantageous in the treatment of disease and abnormal conditions in the body. A careful control of the diet in diabetes mellitus will result in less frequent glycosuria and acidosis, and will enable the patient to maintain a fairly constant blood sugar level with a minimum number of insulin injections.

Anemia is usually treated by a diet that contains additional amounts of iron salts, liver, and vitamins. Diseases of the liver and gallbladder respond more rapidly to a diet that is low in fat and moderately rich in protein. In nephritis, a nearly salt-free diet is fed and the protein intake is restricted. If considerable quantities of protein are lost in the urine, enough protein must be fed to maintain the protein content of the plasma.

Many hospitalized patients are given diets that contain bland, quickly digested foods to prevent upsets and intestinal disturbances from adding to their discomfort. The nature and



Fig. 63. Contrast between two European children, stunted because of inadequate diets, and a well-developed American boy of the same age (eight years). (New York Times, World Wide Photos.)

amount of food given to patients after a major operation are important factors in recovery.

REVIEW QUESTIONS

1. What was your conception of an adequate diet at about the time you started high school?
2. Why has the past war greatly influenced our practical knowledge of nutrition?

3. Which of the three major foodstuffs is used mainly for energy in the diet?
4. Explain the meaning of the following terms: basal metabolism, basal metabolic rate, a basal metabolic rate of 0, and specific dynamic action.
5. How many calories would you estimate the average student nurse requires per day?
6. Why would it be unwise to exist on a lipid-free diet for long periods of time?
7. If your daily calorific requirement was 2250 calories, how many grams of fat would you have to eat to supply your energy requirement? Approximately what fraction of a pound is this amount of fat?
8. Give three examples of an adequate protein. Of an inadequate protein.
9. Why are children fed more than twice the amount of protein per kilogram of body weight than are adults?
10. List the functions of calcium in the body. Of phosphorus.
11. Why are calcium and phosphorus so closely interrelated in nutrition?
12. For what reason is potassium iodide added to the table salt in certain regions of the United States?
13. What are iron and copper used for in the body?
14. List the abnormalities that might occur in the body if the diet lacked sodium and potassium.
15. Why is an adequate diet much more important than the ingestion of multiple vitamin preparations?
16. The nutritional requirements in pregnancy and lactation are similar to those of the growing child. Explain.
17. Briefly discuss three conditions that will respond more favorably when the proper foods are fed to the patient.

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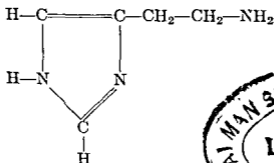
1. What was your conception of an adequate diet at about the time you started high school?
2. Why has the past war greatly influenced our practical knowledge of nutrition?

ologically active compounds called *hormones* that are effective in regulating bodily processes. Hormones are the so-called "chemical messengers" that are produced by endocrine glands and are carried by the blood to some other organ or gland where they exert their effect. The production of hormones by the various endocrine systems are closely interrelated, with the result that there is a harmonious control of the body functions. The hormones will be discussed in connection with the glands that produce them.

HORMONES OF THE DIGESTIVE TRACT

These hormones have been briefly discussed in the chapter on digestion because of their function in the production of digestive juices. The three most important hormones of the digestive tract are *gastrin*, *secretin*, and *cholecystokinin*.

Gastrin is manufactured in the mucosa of the pyloric end of the stomach. The presence of food in the stomach causes this hormone to diffuse into the blood and to stimulate the secretion of gastric juice. Many investigators believe that gastrin is chemically identical to histamine. The injection of histamine causes



Histamine

an increased flow of gastric juice and is often used to collect specimens for gastric analysis.

Secretin is formed in the walls of the duodenum and is liberated into the blood stream whenever the acid gastric contents pass through the pyloric valve. It is carried by the blood to the pancreas, where it stimulates the flow of pancreatic juice. The chemical nature of this hormone is as yet unknown.



CHAPTER XXIV

Hormones

THERE are many glandular organs in the body whose secretions diffuse directly into the blood stream. These are called *ductless glands* because they have no external ducts. They

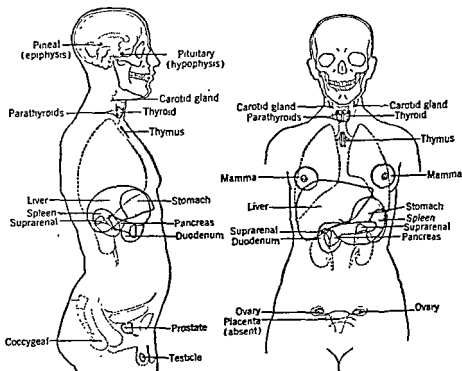


Fig. 64. The location of various endocrine organs in the body. (From Barker, L. F.: Endocrinology and Metabolism. New York, Appleton-Century-Crofts, Inc.)

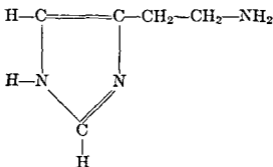
are also often referred to as *endocrine glands* or the *glands of internal secretion*. The secretions of these glands contain physi-

ologically active compounds called *hormones* that are effective in regulating bodily processes. Hormones are the so-called "chemical messengers" that are produced by endocrine glands and are carried by the blood to some other organ or gland where they exert their effect. The production of hormones by the various endocrine systems are closely interrelated, with the result that there is a harmonious control of the body functions. The hormones will be discussed in connection with the glands that produce them.

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Cholecystokinin is also produced in the walls of the duodenum. The presence of fat or acid in this section of the intestine causes this hormone to stimulate the gallbladder to contract and pour bile into the duodenum. Its chemical nature is also unknown.

THE HORMONE OF THE PANCREAS

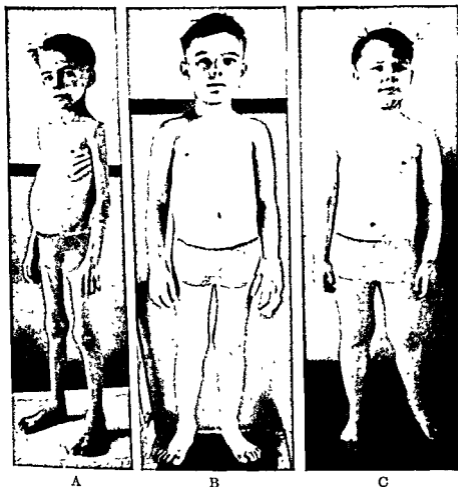
We have already seen that *insulin* is produced by the pancreas and that its main function is to regulate the metabolism of carbohydrates. If this hormone is not produced in sufficient quantity by the pancreas, the disease known as *diabetes mellitus* develops.

Anatomically, the pancreas is made up of two types of tissue, the acinous and the islet tissue. The former produces the pancreatic juice which pours into the intestine through external ducts, whereas the latter is responsible for the formation of insulin.

Although it was demonstrated as early as 1889 that removal of the pancreas of an animal would result in diabetes, it was not until 1922 that Banting and Best developed a method for obtaining active extracts of the pancreas. Within a short time insulin became available in sufficient quantities for the treatment of diabetes. The hormone was crystallized in 1926 and was found to be a protein with a molecular weight of about 35,000. It contains a relatively large amount of the sulfur-containing amino acid, cystine, which is believed to be involved in the physiological activity of insulin. Since it is a protein, it is not effective when taken by mouth, because the proteolytic enzymes of the gastrointestinal tract hydrolyze it and destroy its insulin activity. Insulin is usually injected into the muscles when administered to a diabetic.

The strength of an insulin solution is expressed in units. Originally a *unit of insulin* was one-third the amount of insulin required to decrease the blood sugar level of a 2-kilogram fasting rabbit to a point where the rabbit went into convulsions (45 mg. per 100 cc. of blood). As used today, the unit is somewhat stronger than originally employed. In man, 1 unit of insulin

will cause the oxidation of about 2 gm. of glucose. Crystalline insulin has a potency of 24 units per milligram.



A

B

C

Fig. 65. A diabetic child. A, the loss of weight that occurs in diabetes before insulin therapy is initiated. B and C, the same child two months and one year after treatment was instituted. (From Jeans, P. C., and Rand, W.: *Essentials of Pediatrics*. Philadelphia, J. B. Lippincott Company.)

The main function of insulin is to control the oxidation of glucose in the body. If insulin is injected into the diabetic, the blood sugar level falls, the glycogen storage in liver and muscles increases, and the rate of production of acetone bodies is decreased. The action of insulin is rapid, however, and its effect

soon wears off. This results in variations of the blood sugar level from hour to hour during the day and necessitates frequent injections in severe diabetes. In 1935, Hagedorn combined insulin with protamine (a simple protein) and found that it produced a more prolonged effect on injection. The addition of zinc to protamine insulin still further prolongs the effective action of insulin. Instead of two and three injections a day, many diabetic persons are able to control the blood sugar level with one injection of protamine zinc insulin. However, there are cases in which insulin alone is more effective, for example when severe hyperglycemia must be rapidly reduced to a normal blood sugar level. The protamine zinc insulin may also cause prolonged hypoglycemia that is difficult to overcome.

It should be emphasized that insulin injections will not cure diabetes but will merely allow the diabetic to regulate his carbohydrate metabolism, thus preventing glycosuria, acetone body excretion, acidosis, diabetic coma, and loss of body weight.

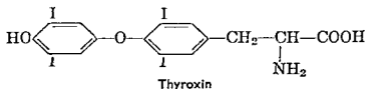
THE HORMONE OF THE THYROID

The Thyroid

The thyroid gland, located on either side of the trachea, consists of two lobes connected by a strip of tissue. It weighs about 20 gm. and its cells are filled with a colloidal material that contains the active principle. This colloid is composed mainly of the protein *thyroglobulin*.

Thyroxin

The hormone of the thyroid gland, *thyroxin*, is a constituent of the protein thyroglobulin. This compound is believed to be made from the amino acid, tyrosine, and has the following structure:



The function of thyroxin is to regulate the rate of metabolism of the body tissues. If extra thyroxin is injected into the body,

the rate of metabolism is increased, the heart beat is increased, and the patient loses weight unless the food intake is increased. Destruction of part of the thyroid by disease results in a slowing down of the metabolic rate and heartbeat and the patient usually becomes sluggish and overweight.

Hypothyroidism

A congenital absence of the thyroid gland or a failure to develop a normal gland in infancy results in *cretinism*. The

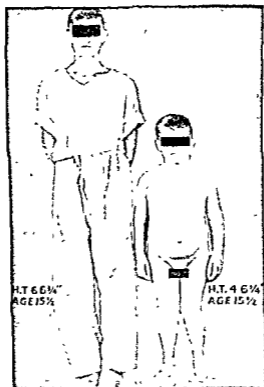


Fig. 66 Comparison of cretin, aged fifteen and one-half years with normal boy of the same age. (From Werner, A. A.: Endocrinology, Clinical Application and Treatment. Philadelphia, Lea & Febiger.)

child grows neither physically nor mentally in a normal fashion but becomes a dwarf with thick dry skin, a wide flat nose, and coarse, scanty hair. Continued treatment with thyroxin, if started at an early age, will cause the child to develop normally.

Hypothyroidism in the adult is called *myxedema* and is characterized by thick dry skin, subnormal temperature and pulse rate, coarse hair, and decreased physical and mental activity. The



Fig. 67. Myxedema. Upper, appearance at height of disease. Lower left, the patient five years before the condition occurred. Lower right, six months after treatment with thyroid extract. (From Hertzler, A. F.: *Diseases of the Thyroid Gland*. New York, Paul B. Hoeber, Inc.)

metabolic rate is lowered and there is a tendency toward increased weight. This condition is also benefited by the injection of thyroxin.

The thyroid gland requires iodine for the manufacture of thyroxin and will not develop properly in the absence of this element. In regions where the iodine content of the soil and drinking water is low, a simple hypothyroidism occurs. In this condition, patients become sluggish and overweight; in general they show symptoms similar to those in myxedema but not as severe.

Hyperthyroidism

In cases of overdevelopment of the thyroid gland, sometimes caused by an *adenoma* or tumor, the gland becomes enlarged and produces excessive amounts of thyroxin. The symptoms in these cases are opposite to those observed in myxedema. The metabolic rate and the heartbeat are increased, the body temperature is above normal, and the patient is usually underweight. Nervous irritability and an increase in mental activity are usually observed. A common symptom of this disease is a bulging of the eyes, which gives it the name *exophthalmic goiter*.

Goiters

The term goiter refers to an enlargement of the thyroid gland, which is evidenced by a swelling in the neck. *Simple goiter*, often called *endemic goiter* or *colloid goiter*, is prevalent in regions of the country where there is a lack of iodine in the crops and drinking water. The thyroid increases in size in an attempt to produce the proper amount of thyroxin. This type of goiter responds favorably to an increase in the iodine intake. Patients suffering from cretinism or myxedema usually have goiters.

The goiters that result from hyperthyroidism are due to an abnormal enlargement of functional thyroid gland tissue which produces excessive amounts of the thyroid hormone. Exophthalmic goiter, for example, is usually treated by surgery or x-ray to remove or destroy part of the gland. In recent years, considerable research on thyroid disorders has been carried out with radioactive iodine. When this radioactive isotope is admin-

istered to the body, it concentrates in the thyroid gland as does ordinary iodine. The radiations given off by the isotope have been found very effective in the treatment of exophthalmic goiter.



Fig. 68. Exophthalmic goiter (Courtesy of Clinics of George W. Crile and Associates: *The Thyroid Gland*. Philadelphia, W. B. Saunders Company.)

THE HORMONE OF THE PARATHYROIDS

The Parathyroids

The parathyroid glands are small organs, weighing about 0.1 gm., which are attached to the thyroid. Two of these are embedded in the thyroid while two others lie on the surface of this gland. Removal of the parathyroids causes death within a few days.

Parathyroid Secretion

The hormone of the parathyroid, *parathyroid secretion*, is probably a protein. Its main function is to maintain a normal level of calcium in the blood. When the parathyroids are removed, the blood calcium decreases and muscle twitches are observed.



Fig. 69. Symptoms of tetany in a child. This condition is caused by a lowered level of calcium in the blood and may be alleviated by injections of parathyroid extract. (From Jeans, P. C., and Rand, W.: *Essentials of Pediatrics*. Philadelphia, J. B. Lippincott Company.)

Within a few days, tetany develops and the patient dies in convulsions. Injections of parathyroid secretion will bring about recovery even when the patient is already in tetany, by transferring calcium from the bones into the blood.

Overactive parathyroids may be caused by an adenoma; this results in increased calcium in the blood with subsequent excre-

tion of this element in the urine. A continuation of this process results in decalcification of the bones, making them soft and weak.

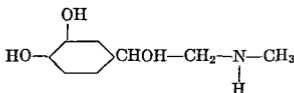
THE HORMONES OF THE ADRENALS

The Adrenals

The adrenals, sometimes called suprarenals, are located on the top of each kidney. They are small glands weighing approximately 3 gm. each. Each adrenal gland consists of two parts, an inner portion called the *medulla* surrounded by an outer layer called the *cortex*.

Epinephrine

The medulla manufactures a hormone known as *adrenalin*, or *epinephrine*. This compound has been prepared synthetically and is a relatively simple substance that is probably made from the amino acid, tyrosine.



Epinephrine

The injection of epinephrine (adrenalin) causes a stimulation of the sympathetic nervous system. The arterioles are constricted and thus cause an increase in blood pressure. The heart muscle is stimulated and the beat is faster than normal. The blood sugar level is increased because the hormone causes glycogenolysis in the liver and muscles; it also causes relaxation of smooth muscle. In general, an injection of epinephrine produces effects similar to those observed in the emotional stress of an emergency.

Epinephrine is frequently injected in patients to counteract insulin shock because of its ability to increase the blood sugar level. It is often mixed with a local anesthetic and injected around the site of an operation to constrict the small blood vessels and check the loss of blood. Epinephrine is useful in combating shock because it produces a temporary increase in the blood pressure. It is sometimes injected directly into the

heart muscle when the heart stops beating during surgical anesthesia. The heart of a newborn baby that is not beating may be started by this method. Small doses of epinephrine are frequently used to relieve the spasm in bronchial asthma by relaxing the muscle of the bronchi.

Hormones of the Cortex

The cortex of the adrenal gland produces a group of hormones known as *cortin*. Several of these hormones have been isolated from the gland and are similar in structure, being derivatives of the sterol nucleus. Two important members of this group are represented as follows:

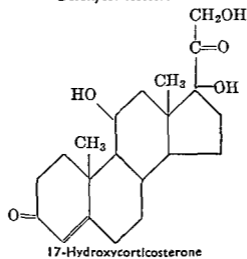
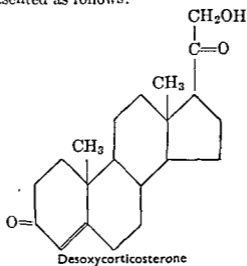




Fig. 70. Addison's disease. Note the areas of extensive pigmentation of the skin. (Loeb, R. F.: Bull. N. Y. Acad. Med., June, 1940.)

Addison's disease results from the failure of the adrenal cortex to produce these hormones. This disease is characterized by

many complex changes in the body. The skin becomes bronze in color, there is loss of weight, extreme muscle fatigue, emaciation, metabolic rate and body temperature are lowered, and the blood volume is decreased. The two most important changes are: (1) a low concentration of sodium and a high concentration of potassium in the blood, accompanied by the excretion of large amounts of sodium in the urine; (2) an improper utilization of carbohydrates, evidenced by a fall in the blood sugar level. The injection of cortin into a patient with Addison's disease results in the alleviation of the above symptoms. Desoxycorticosterone alone corrects the abnormal metabolism of sodium but does not affect the carbohydrate utilization, whereas 17-hydroxycorticosterone is active only in adjusting the metabolism of carbohydrates.

Overactivity of the adrenal cortex may be caused by a cortical tumor and produces an overdevelopment of masculine characteristics in male and female. A man becomes a "paragon of virility" while a woman loses her feminine characteristics and becomes a "masculine caricature of her former self." In children, sexual development occurs at an early age; completely developed secondary sexual characteristics may appear at the age of six.

FEMALE SEX HORMONES

The female sex hormones formed in the ovaries are responsible for the development of the secondary sexual characteristics (development of the breasts, appearance of body hair, and changes in the uterus and vagina) that occur at puberty. These hormones regulate the *estrus cycle* or *menstrual cycle* and function in pregnancy. Before discussing the individual hormones, it may be well to consider the changes that occur in the normal menstrual cycle in women.

The ovaries are small almond-shaped organs that are located in the pelvic cavity on each side of the uterus. At birth, they are filled with numerous immature ova. At puberty, an ovum matures and is discharged into the uterus. In the ovary, the ovum is located in a small spherical-shaped body called the *follicle*. As the ovum matures, the follicle grows and at ovulation it



Fig. 70. Addison's disease. Characterized by darkening of the skin. (Loeb, R. F.: Bull. N. Y. Acad. Med., June, 1940.)

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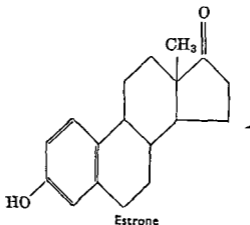
lial lining) sloughs off and is discharged. This process, called *menstruation*, is accompanied by bleeding and continues for four or five days

The entire menstrual cycle may be summarized briefly as follows: Normally, the length of each cycle is four weeks and the days of the cycle are numbered from the onset of menstruation. From the cessation of menstruation until the fourteenth day, the ovum and follicle are maturing in the ovary. During this time, the uterine endometrium is growing under the influence of estrone. Ovulation occurs about the fourteenth day and the ovum is expelled into the uterus. If pregnancy does not occur, the corpus luteum that develops in the ovary disappears after about a week. The endometrium is maintained by progesterone until menstruation occurs and removes the endometrium from the uterus. The cycle then repeats itself.

If pregnancy occurs, the corpus luteum continues to develop, preventing further ovulation or menstruation.

Hormones of the Follicle

The liquid within the follicle contains at least two hormones, known as *estrone* and *estradiol*. Estrone (theelin) was the first principle to be isolated from the follicular liquid; however estradiol (dihydrotheelin) is more potent than estrone and may be the principal hormone. These compounds are related chemically to the sterols



ruptures to release the ovum. During the development of the follicle, the hormone *estrone* is produced.

After the follicle ruptures, it first fills with blood, then is replaced by large yellow cells forming the *corpus luteum* (yellow body). A second hormone, *progesterone*, is formed in the corpus luteum. If the discharged ovum is not fertilized by spermatozoa in the uterus, the *corpus luteum* is soon replaced by scar tissue. If pregnancy occurs, however, this gland is active throughout

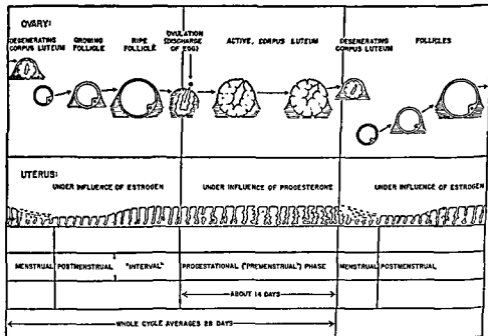
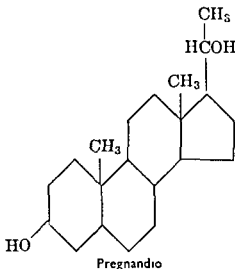


Fig. 71. The sequence of events in the menstrual cycle. (From Corner, G. W.: *The Hormones in Human Reproduction*. Princeton University Press.)

the period of pregnancy. This process of ovulation and development of the corpus luteum is repeated every four weeks in a normal woman, if pregnancy does not occur.

Prior to ovulation, changes are also occurring in the uterus. The walls and epithelial lining of the uterus become thicker in preparation for the implantation of the fertilized ovum. If the ovum is not fertilized, the lining of the uterus is maintained for about two weeks after ovulation, then the endometrium (epithe-



The Hormone of the Corpus Luteum

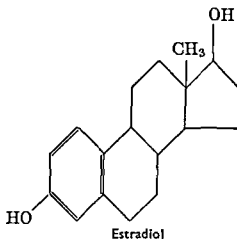
The hormone produced by the corpus luteum is called *progesterone*. In the body, progesterone is converted into *pregnan-20-one* by reduction, before it is excreted in the urine. These two compounds are similar to the estrogens in chemical structure.

The main function of progesterone is the preparation of the uterine endometrium for implantation of the fertilized ovum. If pregnancy occurs, this hormone is responsible for the retention of the embryo in the uterus and for the development of the mammary glands prior to lactation.

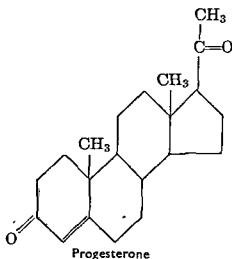
During the early stages of pregnancy, a round, flat organ called the *placenta* is formed in the uterus. The placenta is the attachment between the mother and the fetus. The placenta produces hormones during pregnancy, especially estrone and a hormone that inhibits the continuance of the normal menstrual cycle.

MALE SEX HORMONES

The male sex hormones are produced by the testes, which are two oval glands located in the scrotum of the male. Small glands in the testes form spermatozoa which are capable of fertilizing a mature ovum. Between the cells that manufacture spermatozoa are the *interstitial cells* which produce a hormone called *testos-*



These two compounds are excreted in the urine in increased amounts during pregnancy. Similar compounds such as *estriol* have been isolated from urine during pregnancy, although their estrogenic activity is low compared to the follicular hormones. As has already been stated, the function of the estrogens is the development of the secondary sexual characteristics at puberty and the regeneration of the endometrium of the uterus in the first half of the menstrual cycle.



If the testes are removed before puberty, masculine characteristics fail to develop, the voice is high pitched, the beard fails to grow, and the fat deposition of the body resembles that of the female. The castration of young animals is commonly practised in the raising of livestock. Such animals put on weight more rapidly and produce a higher quality of meat.

HORMONES OF THE PITUITARY

The Pituitary Gland

The pituitary gland (hypophysis) is a small organ that is located at the base of the brain. It is composed of an *anterior lobe* and a *posterior lobe*, which are connected by a strip of tissue known as the *pars intermedia*. The anterior lobe produces several hormones that are necessary for the proper functioning of the other endocrine glands. For this reason, the anterior lobe of the pituitary is often referred to as the master gland of the endocrine system. Since the two lobes form different hormones, they will be discussed separately.

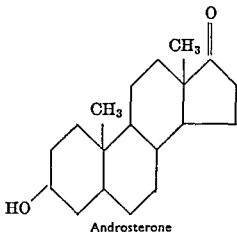
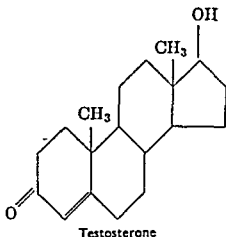
Hormones of the Anterior Lobe

The hormones of the anterior lobe are protein in nature and are therefore not characterized chemically as are many of the other hormones. Many physiological functions have been attributed to this gland. However, we will confine our discussions to those that exhibit a definitely accepted function.

Growth Hormone. This principle of the anterior lobe controls the growth of young animals. If the hormone is lacking in childhood, the individual becomes a dwarf. The familiar circus dwarf is usually the result of pituitary insufficiency. In contrast to the cretins, these dwarfs have well-formed bodies and normal intellect.

An excessive formation of the growth hormone in childhood may result from an adenoma of the gland, and causes gigantism. Most of the giants seen in the circus probably had an overactive pituitary during their childhood. If this hormone is produced in excessive amounts in an adult, the condition of *acromegaly* develops. Acromegaly (Fig. 72) is characterized by an increased

Testosterone. This hormone is probably converted into other compounds such as *androsterone* before being excreted in the urine. *Dehydroandrosterone* has also been isolated from male urine but is much less active than the other two hormones. The male sex hormones or *androgens* have structures similar to the estrogens.



The main function of the androgens is the development of masculine sexual characteristics, such as deepening of the voice, the growth of a beard, and distribution of body hair at puberty. They also control the function of the glands of reproduction (seminal vesicles, prostate, and Cowper's gland).

If the testes are removed before puberty, masculine characteristics fail to develop, the voice is high pitched, the beard fails to grow, and the fat deposition of the body resembles that of the female. The castration of young animals is commonly practised in the raising of livestock. Such animals put on weight more rapidly and produce a higher quality of meat.

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disproportional growth of the bones in the face, hands, and feet.

Gonad-stimulating Hormones. The ovaries in women, and testes in men, are sometimes called the gonads. The anterior pituitary contains substances that regulate the formation of sex hormones. The *follicle-stimulating hormone* controls the growth of the follicles and stimulates the production of follicular hormones. In the male, this hormone regulates the function of the cells that make spermatozoa. The formation of corpus luteum and progesterone are stimulated by the *lutinizing hormone*,

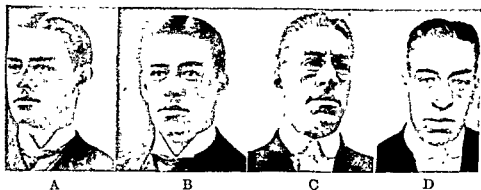


Fig. 72. Acromegaly. A, the patient at age twenty-four before the development of the symptoms; B, at age twenty-nine, first evidence of symptoms; C, at age thirty-seven; and D, at age forty-two, when acromegaly is definite. (From Cushing: *The Pituitary Body and Its Disorders*. Philadelphia, J. B. Lippincott Company.)

while in the male this factor controls the production of androgens by the interstitial cells of the testes. The different stages of the menstrual cycle and the normal course of pregnancy depend on the balance between these two hormones.

Lactogenic Hormone. This hormone, called *prolactin*, has been isolated in a crystalline form. Prolactin is a protein that initiates lactation. During pregnancy this hormone is inhibited by the principle in the placenta that stimulates the growth of the mammary glands. When the placenta is removed, the prolactin is free to stimulate milk formation, and lactation occurs.

Thyrotropic Hormone. The development and secretion of the thyroid gland is stimulated by the thyrotropic hormone. If the

anterior lobe of the pituitary is removed, the thyroid atrophies and fails to produce sufficient thyroxin, thereby causing a drop in the metabolic rate. When extracts of this hormone are injected into experimental animals, the thyroid gland enlarges and a condition similar to exophthalmic goiter is produced.

Adrenotropic Hormone. This hormone stimulates the growth and function of the adrenal cortex. Some cases of Addison's

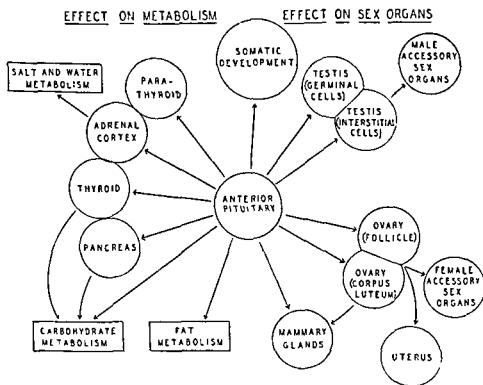


Fig 73. The relation between the anterior pituitary and the sex organs and metabolism in the body.

disease have benefited more from injections of this factor than from cortin itself.

Pancreatropic Hormone. Extracts of the anterior lobe of the pituitary when injected into animals cause an increased production of insulin by the pancreas. Continued injections result in an exhaustion of the islet tissue and insulin formation decreases markedly. Experimental animals have been made per-

- 5 How many units of insulin would a diabetic require if he oxidized an amount of carbohydrate equivalent to 100 gm. of glucose in a day?
6. What advantages does the use of protamine zinc insulin have over ordinary insulin? What disadvantages?
7. At one time preparations containing thyroxin were used for removal of excess body weight. How would the hormone accomplish this? Can you suggest a reason for the fact that it is not used for this purpose today?
8. Name and describe the conditions that result from hypothyroidism. From hyperthyroidism.
9. Is there a logical connection between the parathyroid gland and bone formation? Explain. Why is tetany sometimes observed in cases of rickets?
10. Name five uses of epinephrine in medicine.
11. What disease results from the lack of function of the adrenal cortex? What are the outstanding symptoms of this disease?
12. A hyper function of the adrenal cortex produces what condition in men? In women? In children?
- 13 Explain the following terms: estrus cycle, follicle, corpus luteum, and menstrual cycle.
14. What process occurs at ovulation? At menstruation?
- 15 Why do ovulation and menstruation cease when pregnancy occurs?
16. What are the main functions of the estrogens? Of progesterone?
17. Name two androgens and give their main functions.
- 18 Why is the anterior lobe of the pituitary gland often called the master gland of the endocrine system?
19. What similarities exist in the conditions caused by a lack of the growth hormone in childhood and hypothyroidism in infancy? What differences?
20. Why are the gonad stimulating hormones important in reproduction?
21. Compare the activity of the pancreatropic and the diabetogenic hormones?
- 22 Pitocin is often injected immediately before or immediately after childbirth. Explain its use in both cases.
23. Why is pitressin sometimes used to combat shock?

manently diabetic by this factor, therefore it may also be called the diabetes-producing hormone.

Diabetogenic Hormone. This hormone stimulates the breakdown of liver glycogen and causes an increase in the blood sugar level. If the anterior lobe of the pituitary is removed from a diabetic animal there is a temporary lowering of the blood sugar level due to the lack of the diabetogenic hormone.

Hormones of the Posterior Lobe

The posterior lobe of the pituitary gland produces at least two hormones, *pitocin* and *pitressin*. Pitocin or *oxytocin* is a factor that causes a contraction of the smooth muscle of the uterus when it is injected. This hormone is often used in obstetrics to contract the uterus after the birth of the child and thus aid in the control of hemorrhage.

Pitressin or *vasopressin* stimulates the peripheral blood vessels and causes a gradual, prolonged increase in blood pressure. It is sometimes used instead of epinephrine to combat shock, because of its prolonged effect. Pitressin also controls the formation of urine. Injection of this substance in a patient with diabetes insipidus greatly decreases the urine volume. It is believed to influence the process of reabsorption of water by the kidney tubules.

The Pars Intermedia

This small strip of tissue produces a hormone that increases the size of the pigment spots on the skin of frogs and fish but has not been shown to function in the human.

REVIEW QUESTIONS

1. Why are the endocrine glands also called ductless glands and glands of internal secretion?
2. Name the three main hormones of the digestive tract. What is the function of each hormone in digestion?
3. Why are gastrin and histamine thought to be the same compound?
4. Many attempts have been made to find a substance that can be taken by mouth and still retain the physiological activity of insulin. Why do such attempts always end in failure?

- 5 How many units of insulin would a diabetic require if he oxidized an amount of carbohydrate equivalent to 100 gm. of glucose in a day?
6. What advantages does the use of protamine zinc insulin have over ordinary insulin? What disadvantages?
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- 22 Pitocin is often injected immediately before or immediately after childbirth. Explain its use in both cases.
- 23 Why is pitressin sometimes used to combat shock?

Appendix

INTERNATIONAL ATOMIC WEIGHTS (1947)

Element	Symbol	Atomic Number	Atomic Weight	Element	Symbol	Atomic Number	Atomic Weight
Aluminum	Al	13	26.97	Molybdenum	Mo	42	95.95
Antimony	Sb	51	121.76	Neodymium	Nd	60	144.27
Argon	A	18	39.944	Neon	Ne	10	20.183
Arsenic	As	33	74.91	Nickel	Ni	28	58.69
Barium	Ba	56	137.36	Nitrogen	N	7	14.008
Beryllium	Be	4	9.02	Osmium	Os	76	190.2
Bismuth	Bi	83	209.00	Oxygen	O	8	16.0000
Boron	B	5	10.82	Palladium	Pd	46	106.7
Bromine	Br	35	79.916	Phosphorus	P	15	30.98
Cadmium	Cd	48	112.41	Platinum	Pt	78	195.23
Calcium	Ca	20	40.08	Potassium	K	19	39.098
Carbon	C	6	12.010	Praseodymium	Pr	59	140.92
Cerium	Ce	58	140.13	Protactinium	Pa	91	231
Cesium	Cs	55	132.91	Radium	Ra	88	226.05
Chlorine	Cl	17	35.457	Radon	Rn	86	222
Chromium	Cr	24	52.01	Rhenium	Re	75	186.31
Cobalt	Co	27	58.94	Rhodium	Rh	45	102.91
Columbium	Cb	41	92.91	Rubidium	Rb	37	85.48
Copper	Cu	29	63.54	Ruthenium	Ru	44	101.7
Dysprosium	Dy	66	162.46	Samarium	Sm	62	150.43
Erbium	Er	68	167.2	Scandium	Sc	21	45.10
Europium	Eu	63	152.0	Selenium	Se	34	78.96
Fluorine	F	9	19.00	Silicon	Si	14	28.06
Gadolinium	Gd	64	156.9	Silver	Ag	47	107.880
Gallium	Ga	31	69.72	Sodium	Na	11	22.997
Germanium	Ge	32	72.60	Strontium	Sr	38	87.63
Gold	Au	79	197.2	Sulfur	S	16	32.066
Hafnium	Hf	72	178.6	Tantalum	Ta	73	180.88
Helium	He	2	4.003	Tellurium	Te	52	127.61
Holmium	Ho	67	164.94	Terbium	Tb	65	159.2
Hydrogen	H	1	1.0080	Thallium	Tl	81	204.39
Indium	In	49	114.76	Thorium	Th	90	232.12
Iodine	I	53	126.92	Thulium	Tm	69	169.4
Iridium	Ir	77	193.1	Tin	Sn	50	118.70
Iron	Fe	26	55.85	Titanium	Ti	22	47.90
Krypton	Kr	36	83.7	Tungsten	W	74	183.92
Lanthanum	La	57	138.92	Uranium	U	92	238.07
Lead	Pb	82	207.21	Vanadium	V	23	50.95
Lithium	Li	3	6.940	Xenon	Xe	54	131.3
Lutetium	Lu	71	174.99	Ytterbium	Yb	70	173.04
Magnesium	Mg	12	24.32	Yttrium	Y	39	88.92
Manganese	Mn	25	54.93	Zinc	Zn	30	65.38
Mercury	Hg	80	200.61	Zirconium	Zr	40	91.22

EXPLANATION OF PERIODIC TABLE (p. 325)

For a more complete explanation of the table on page 325 several important relationships

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Cobalt	Co	27	58.94	Rhodium	Rh	45	102.91
Columbium	Cb	41	92.91	Rubidium	Rb	37	85.48
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Erbium	Er	68	167.2	Scandium	Sc	21	45.10
Europium	Tu	63	152.0	Selenium	Se	34	78.96
Fluorine	F	9	19.00	Silicon	Si	14	28.06
Gadolinium	Gd	64	156.9	Silver	Ag	47	107.880
Gallium	Ga	31	69.72	Sodium	Na	11	22.997
Germanium	Ge	32	72.60	Strontium	Sr	38	87.63
Gold	Au	79	197.2	Sulfur	S	16	32.066
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Manganese	Mn	25	54.93	Zinc	Zn	30	65.38
Mercury	Hg	80	200.61	Zirconium	Zr	40	91.22

EXPLANATION OF PERIODIC TABLE (p. 325)

When the elements are grouped as shown in the table on page 325, a few important facts may be noted:

CHEMICAL PROPERTIES OF THE IMPORTANT ELEMENTS

Element	Outstanding Properties	Preparation by					Industrial Uses of Compounds
		Reduction of Sulfide	Reduction of Oxide	Electrolysis	Occurs Free	Liquid Air	
Metals	Sodium Potassium Calcium						Glass, soap, paper, soda Photography, fertilizers Plaster of paris, cement, glass
	Magnesium Zinc						Alloys, asbestos, talc, dyes Galvanized iron, alloys, paint
	Arsenic Bismuth						Insecticides, glass, dyes Type metal, ballpoint metal
	Iron Nickel Tin						Construction, blue prints Alloys, hydrogenation of oils Solder, dyes
	Lead Copper Mercury Silver						Paint, storage batteries, alloys Conductors, alloys, fruit sprays Explosives, illumination Photography, mirrors
	Gold Platinum						Dentistry alloys, jewelry X-ray tubes, dental alloys
	Aluminum Manganese Chromium						Alloys, electric conductors, paint Alloys, dry-cell batteries Chrome plating, pigments
	Radium						Luminous materials
	Hydrogen Oxygen						Ammonia, hydrogenating oils Oxyacetylene torches
	Nitrogen Neon						Ammonia, explosives, fertilizers Illumination
Non-metals	Phosphorus Fluorine Chlorine Bromine Iodine						Matches, fertilizers Etching of glass, catalysts Purifying of water, bleaching Dyes, gasoline, photography Dyes, photography
	Sulfur Carbon						Acids, dyes, paper pulp Rubber products, phonograph records
	Silicon						Cement, glass, carborundum

PERIODIC TABLE—Continued

Period	Group 0	Group I	Group II	Group III	Group IV	Group V	Group VI	Group VII	Group VIII
6	86 Rn 222	87 Fr 223	88 Ra 226.05	89 Ac 227.05	90**				
5	*58-71 Rare Earths		83 Ce 140.13	89 Pr 140.92	90 Nd 144.27	91 Pm ?	92 Sm 150.43	93 Eu 152	64 Gd 158.9
			85 Tb 159.2	86 Dy 162.40	87 Ho 163.5	88 Er 167.2	89 Tm 169.4	90 Yb 173.04	71 Lu 174.99
6	**90-98 Rare Earths		90 Th 232.12	91 Pa 231	92 U 238.07	93 Np 237	94 Pu 239	95 Am 241	96 Cm 242

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BIOLOGICAL SIGNIFICANCE OF THE IMPORTANT ELEMENTS

Element	Per Cent in Earth's Crust	Per Cent in Human Body	Occurrence in Body				Medical Uses of Compounds
			Bones and Teeth	Enzymes	Muscle	Blood	
Essential in Diet	Calcium	3.39	2.0				In rickets, tetany
	Carbon	0.08	15.0				In all organic compounds
	Chlorine	0.19	0.15				Germicides, anesthetics
	Cobalt	Trace				For hematopoiesis
	Copper	0.03	0.00015				Germicides; hematopoiesis
	Fluorine	0.03	Trace				Blood anticoagulants
	Hydrogen	0.87	10.0				In organic compounds
	Iodine	0.00004	0.00004				Germicides; in goiter
	Iron	4.71	0.004				In anemia, astringents
	Magnesium	1.93	0.03				Antacids, cathartics
	Manganese	0.09	0.0003				Antiseptics
	Nitrogen	0.03	3.0				Constituent of proteins
Non-essential	Oxygen	43.20	63.0				Gas used in anoxias
	Phosphorus	0.11	1.1				Cathartic; lead poisoning
	Potassium	2.40	0.35				Making soluble salts
	Sodium	2.63	0.15				Making soluble salts
	Sulfur	0.06	0.25				Skin diseases; germicides
	Zinc	Trace	Trace				With insulin; astringents
	Aluminum	7.50	Trace				Antacids, astringents
	Antimony	..	Trace				Parasitocides, emetics
	Arsenic	..	Trace				In syphilis, leukemia
	Barium	0.04	..				X-ray, antidiarrhetics
	Bismuth	..	Trace				Antisyphilitic, adsorbents
	Boron	..	Trace				Disinfectants, protectives
Non-essential	Bromine	Trace	Trace				Sedatives, blood dyes
	Gold	Trace	Trace				Arthritis
	Lead	Trace	Trace				Astringents
	Mercury	0.03	Trace				Antisyphilitics, germicide
	Nickel	Trace	Trace				Toxic
	Radium	Trace	Trace				Destruction of carcinomas
Non-essential	Selenium	Trace	Trace				Toxic
	Silicon	28.06	Trace				Antacids

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BIOLOGICAL SIGNIFICANCE OF THE IMPORTANT ELEMENTS

Element	Per Cent in Earth's Crust	Per Cent in Human Body	Occurrence in Body				Medical Uses of Compounds
			Bones and Teeth	Enzymes	Muscle	Blood	
Essential in Diet	Calcium	3.39	2.0				In rickets, tetany
	Carbon	0.04	18.0				In all organic compounds
	Chlorine	0.19	0.15				Germicides, anesthetics
	Cobalt	Trace				For hematopoiesis
	Copper	0.00015				Germicides, hematopoiesis
	Fluorine	0.03	Trace				Blood anticoagulants
	Hydrogen	0.87	10.0				In organic compounds
	Iodine	0.00004				Germicides; in goiter
	Iron	4.71	0.004				In anemia, astringents
	Magnesium	1.93	0.05				Antacids, cathartics
Non-essential	Manganese	0.09	0.0003				Antiseptics
	Nitrogen	0.03	3.0				Constituent of proteins
	Oxygen	49.20	65.0				Gas used in anoxias
	Phosphorus	0.11	1.1				Cathartic; lead poisoning
	Potassium	2.40	0.35				Making soluble salts
	Sodium	2.63	0.15				Making soluble salts
	Sulfur	0.06	0.25				Skin diseases; germicides
	Zinc	Trace				With insulin; astringents
	Aluminum	7.50	Trace				Antacids, astringents
	Antimony	...	Trace				Parasitocides, emetics
	Arsenic	...	Trace				In syphilis, leukemia
	Barium	0.04	...				X-ray, antidiarrhetics
	Bismuth	...	Trace				Antisyphilitic, adsorbents
	Boron	...	Trace				Disinfectants, protectives
	Bromine	...	Trace				Sedatives, blood dyes
	Gold	...	Trace				Arthritis
	Lead	...	Trace				Astringents
	Mercury	...	Trace				Antisyphilitic, germicide
	Nickel	0.02	Trace				Toxic
	Radium	...	Trace				Destruction of carcinomas
	Selenium	23.06	Trace				Toxic
	Silicon	...	Trace				Antacids

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